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2 Gross, Elmer R., M.D.; Howles, James K., M.D.; Non-Specific Treatment of Dermatoses and Adjunctive Therapy of Syphilis with Oral Sodium Bismuth Triglycollamate. Read before the Section of Dermatology and Syphilology Meeting of the Centennial Meeting of the A.M.A. at Atlantic City, New Jersey, June 12, 1947.

3 Year Book of Dermatology and Syphilology, 1946, page 31.

4 Sawicky, H. H., M.D.; Bistrimate (sodium bismuth triglycollamate) Administered by Mouth in the Treatment of Chronic Discoid Lupus Erythematosus. The Journal of Investigative Dermatology, vol. 9 #3 September 1947.

5 Howles, James K., M.D.; Treatment of Inflammatory-Dermatoses with Oral Bismuth (sodium bismuth triglycollamate). Southern Medical Journal, vol. 41 #11, pages 1033-1041, November 1948.

6 Pascher, Frances, M.D.; Sawicky, H. H., M.D.; Silverberg, M.G., M.D.; and Emmet, Richard, M.D.; Bistrimate for Lupus Erythematosus, Lichen Planus and other Dermatoses. Journal of Investigative Dermatology, vol. 10, #6, June 1948.

7 Miller, Thomas H., M.D. and Delaney, James R., M.D.; Oral Bismuth therapy in Dermatology. Archives of Dermatology and Syphilology, Vol. 60, August 1949.

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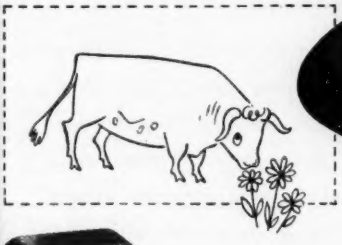

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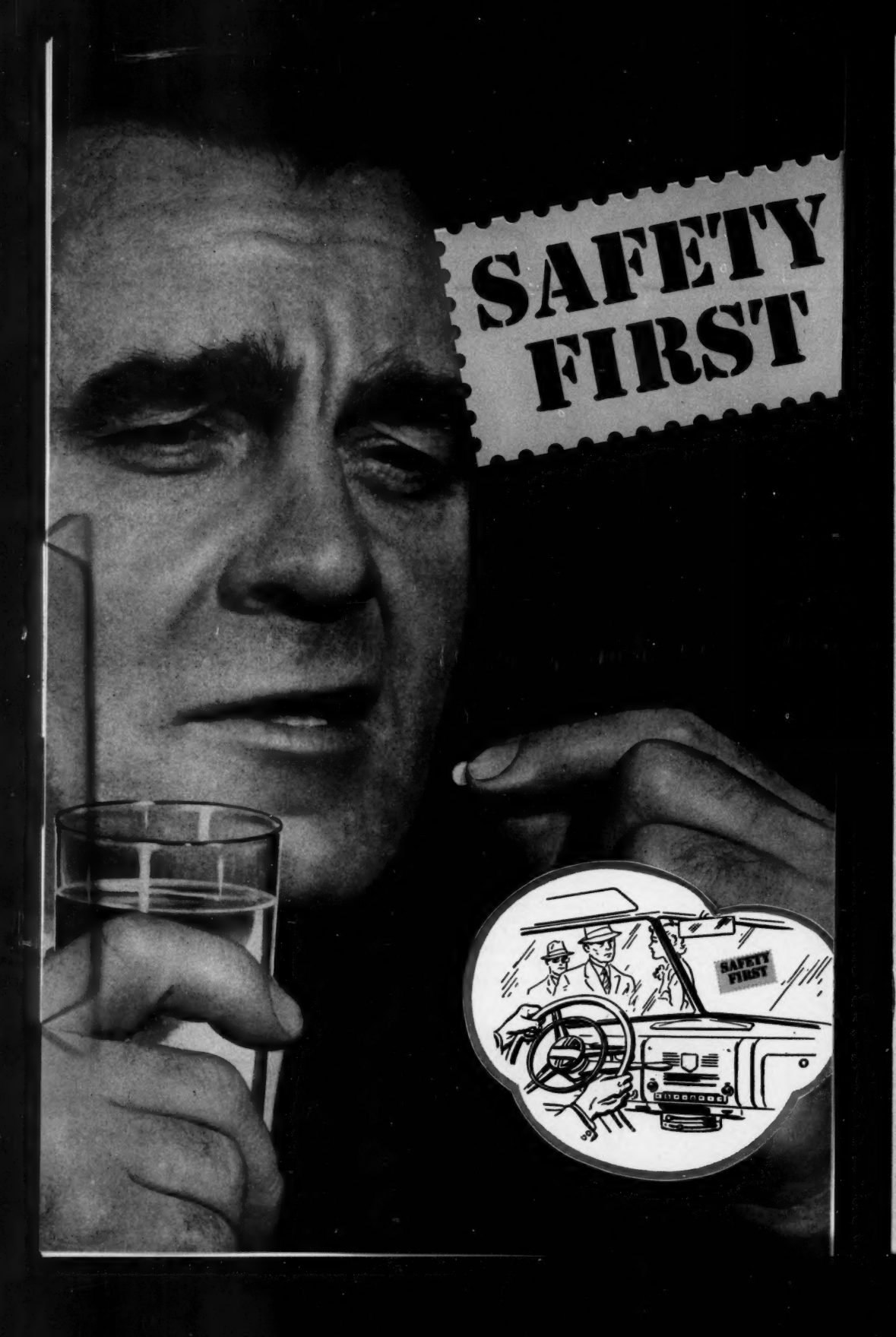
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References: 1. Feinberg, S. M.: Ann. N. Y. Acad. Sci. 50:1186 (April) 1950. 2. Landis, C. and Zubin, J.: J. Psychology 31:181 (April) 1951. 3. Schwartz, E.: Ann. Allergy 7:770 (Nov.-Dec.) 1949. 4. Sherman, W. B.: Bull. N. Y. Acad. M. 27:309 (May) 1951.

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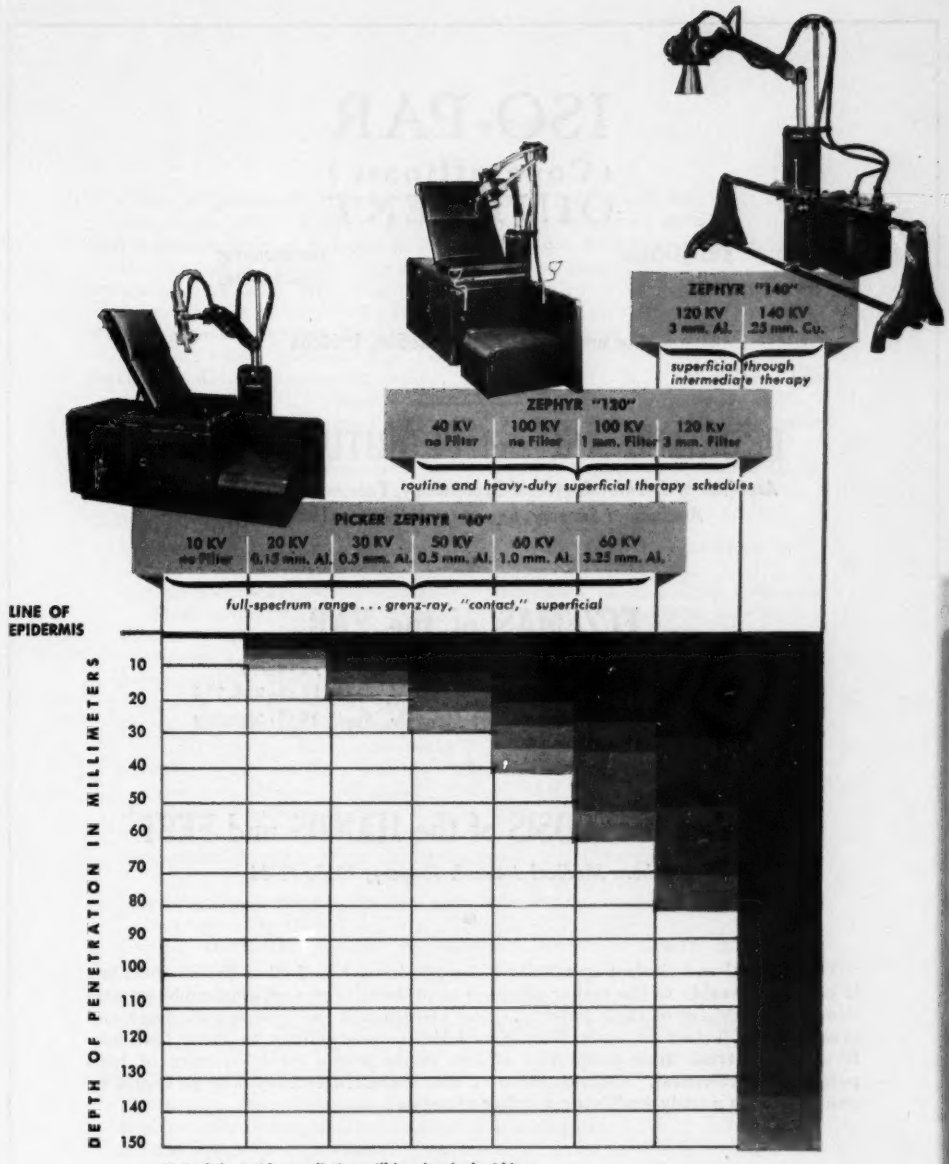

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A. M. A.
Archives of Dermatology and Syphilology

VOLUME 64 JULY 1951 NUMBER 1

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PROGNOSIS OF DERMATITIS HERPETIFORMIS, TREATED AND UNTREATED

WILLIAM H. EYSTER Jr., M.D.
AND
ROBERT R. KIERLAND, M.D.
ROCHESTER, MINN.

SINCE dermatitis herpetiformis was recognized by Duhring[1] in 1884 and separated from other bullous diseases, few reports have been made concerning the natural course of the disease. Duhring himself was indefinite as to the course of the disease, stating that he believed some patients had recovered but that he had known of cases in which the condition endured for 5, 10 and 15 years. The disease has been generally accepted as being chronic and of unkown etiology and as running a long and erratic course. Because of this gap in our knowledge of this not uncommon dermatosis, a survey of the records of the Mayo Clinic was undertaken and follow-up information was sought by letter in an attempt to discover the natural course of the disease and the effect of treatment.

MATERIAL

The records of all patients who were given a clearcut diagnosis of dermatitis herpetiformis were examined. Patients seen in the 20 year period from 1920 through 1939 were selected in order that a minimum of 10 years might be covered by the follow-up inquiry. In most of the original records notations were made concerning the severity of the process at the time of examination. Four grades of severity were found: "mild," "moderately severe," "severe" and, finally, an extremely severe type which was classed as the "erythema multiforme-dermatitis herpetiformis-pemphigus" type of eruption. In all the patients with this last condition who were followed for a time, the disorder was eventually diagnosed as dermatitis herpetiformis, and their cases were included in this study.

GENERAL INCIDENCE

Dermatitis herpetiformis has been described as a rare disease, and yet in the 20 year period covered in our study a total of 381 patients were seen whose dermatosis was diagnosed as dermatitis herpetiformis. The cases with questionable diagnosis and the marginal cases were excluded from the series. In the period covered by the study a total of approximately 200,000 patients with dermatologic conditions were examined. Thus, one patient with dermatitis herpetiformis was seen among every 500 with dermatologic complaints. There appears to have been relatively little change in the incidence of the disease from 1930 to the present.

Fellow in Dermatology and Syphilology, Mayo Foundation (Dr. Eyster), and the Section on Dermatology and Syphilology, Mayo Clinic (Dr. Kierland).

1. Duhring, L. A.: Selected Monographs on Dermatology, London, The New Sydenham Society, 1893.

INCIDENCE BY SEX

Search of current textbooks of dermatology and a survey of the literature failed to reveal definite information on the incidence of dermatitis herpetiformis according to the sex of the patient. Ormsby and Montgomery [2] simply stated that it occurs in both sexes, and Becker and Obermayer [3] stated that it is more frequent in men. Of our group of 381 patients, 279 were males and 102 were females, a ratio of men to women of 2.7 to 1. There was apparently little significant variation in the degree of severity according to sex except among patients who had severe eruptions which before observation were classified as belonging to the "erythema multiforme-dermatitis herpetiformis-pemphigus" group. There were 11 patients in this group, eight of whom were women. Thus the ratio in this group is an exact inversion of the over-all ratio of men to women with dermatitis herpetiformis.

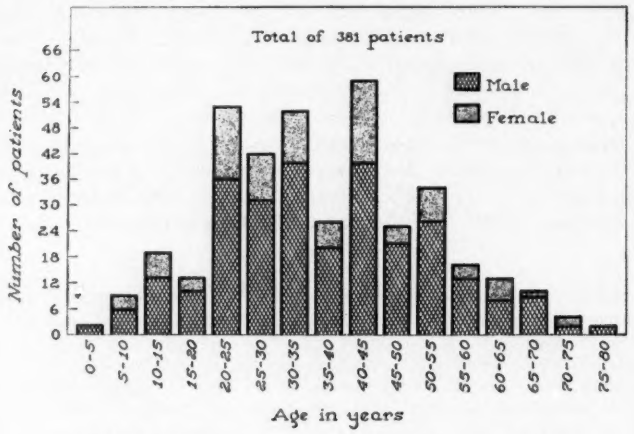

Fig. 1.—Patients' age at the onset of dermatitis herpetiformis.

AGE OF ONSET

Definite information as to the age of onset of dermatitis herpetiformis also is scanty in the literature; statements such as "adult" and "all ages but most common in the adult" seem to suffice. Reports of isolated cases indicate the infrequent incidence of dermatitis herpetiformis in children less than 10 years of age. Søbye [4] reported on 21 children in whom the age at onset was between 1 and 14 years.

In our study the earliest onset noted was that in two male infants whose difficulty began at the age of 6 months. The earliest onset in females in our group was at 7 years of age. On the other hand, one man in our series was 78 years

2. Ormsby, O. S., and Montgomery, Hamilton: Diseases of the Skin, ed. 7, Philadelphia, Lea & Febiger, 1948.

3. Becker, S. W., and Obermayer, M. E.: Modern Dermatology and Syphilology, ed. 2, Philadelphia, J. B. Lippincott Company, 1947.

4. Søbye, P.: The Prognosis of Herpetiform Dermatitis in Children, Acta dermat.-venereol. **28**:262-269, 1948.

old at the time of onset, and a women patient 71 years old. The ages of all the patients at the onset of the disorder were recorded. For convenience the ages were grouped according to five-year intervals (fig. 1). The disease in 61 per cent of the patients began between the ages of 20 and 45 years and in 77 per cent between the ages of 20 and 55 years. The incidence of the disease was much less in the younger and older age groups. Thus the times of onset of the disease correspond to the periods of greatest activity in adult life.

The age of onset had apparently little relation to the future course of the disease. In patients of all age groups except those whose disease began late in life, the duration of the disease was found to be both relatively short (one to five years) and relatively long (20 to 30 years). The duration of the disease in the older groups was of course limited by the natural life span. Of the four categories previously defined, only in the erythema multiforme-dermatitis herpetiformis-pemphigus group was there any variation in the age of onset. In 60 per cent of the patients who had the mild form of the disease and in 50 per cent of those with

TABLE 1.—*Duration of Dermatitis Herpetiformis*

Present Status of Disease	Duration of Disease, Years, with No. of Patients									Total
	0-5	6-10	11-15	16-20	21-25	26-30	31-35	36-40	41-45	
In remission	13	20	15	9	8	4	1	0	2	72
Present but milder	0	0	19	13	12	8	3	2	2	59
As severe as originally	0	6	9	15	11	2	3	2	0	48
Patient dead; disease present until death	4	6	4	2	4	3	0	1	0	24
Total no. of patients traced to March 1950										203
Undetermined in 1950 but known to have been present for years	5	25	5	7	3	1	0	0	0	46
Total followed	22	57	52	46	28	18	7	5	4	249
Patients dead; status of disease undetermined										27
Undetermined										105
Total										381

the severe form the onset was between the ages of 20 and 45 years. In only 21 per cent of the patients in the erythema multiforme-dermatitis herpetiformis-pemphigus group, however, did the onset of the difficulty occur between the ages of 20 and 45 years, whereas in 78 per cent of this group the disorder began after the age of 40 years.

COURSE AND PROGNOSIS

As mentioned earlier, notations were made on the severity of the disease in most persons. In many cases seasonal variations were noted, eosinophilia of the peripheral blood was found and sensitivity to halogens was revealed by various patch tests. The follow-up studies provided us with information on the course and prognosis of the dermatosis after each patient's last visit to the clinic.

Of the 381 patients on whom this report is based, 203 were traced to March 1950. Of the remainder, 27 were known to be dead but the status of the skin disease was unknown after they left the clinic, and 46 were traced for some time, ranging from four to 25 years, but not to March 1950. Thus definite information is available on the course of the disease in 249 patients (table 1).

Of the original 381 patients 33 had mild, 307 moderately severe, 30 severe and 11 very severe (the "erythema multiforme-dermatitis herpetiformis-pemphigus"

type) dermatitis herpetiformis. These classifications were subject to the judgment of the individual physicians at the time the patients were seen. Of the 33 patients who had the mild form of the disease 21 per cent had had the condition for more than 10 years and were gradually reaching the quiescent stage at the time of examination and diagnosis at the clinic. The remainder complained of symptoms of less than 10 years' duration and some of only one year or less. In the group with the severe form of the disease one patient had had dermatitis herpetiformis for 40 years and another for 30 years. Of the patients with the severest form one had had the disorder for 12 years. These observations demonstrate that the tendency of the disease is to begin in a severe form and gradually taper off into a milder form and then eventually disappear; however, the disease of many is mild at onset and remains so. That of others begins in a severe form and remains severe for long periods—up to 40 years.

From the information obtained from the follow-up studies it became apparent that there was no correlation between the degree of severity of the disease when the patient was seen at the clinic and the future course of the disease. Follow-up studies also indicated that in all four groups of severity the disease may last from two to 40 years, with no group showing a significantly higher number of remissions than any other group.

Thirty-five per cent of the persons who were followed to March 1950 reported their disease in remission. The shortest reported duration of active dermatitis herpetiformis was two years; the patient in this case further reported that his disorder had been in remission for 14 years. Two patients reported that they had had dermatitis herpetiformis for more than 40 years before a remission of several years' duration developed.

Twenty-nine per cent of the group traced to March 1950 reported that they still had dermatitis herpetiformis but that their symptoms were much less severe and less frequent than at the onset of their disease. They reported that the symptoms had gradually tapered off. This amelioration apparently began 10 to 20 years after the onset of the disease in the majority of the patients. Twenty-four per cent of the patients answering concerning the present status of their disease reported their symptoms just as severe and attacks just as frequent as they had been at the onset of their difficulties. Most of the patients so reporting had had the disorder less than 25 years, and only 18 so reporting had had the condition more than 20 years. Twelve per cent were dead; the skin disorder had still been present at time of death, from three to 40 years after its onset.

It may be inferred from these reports that dermatitis herpetiformis is a chronic disease which retains its original intensity for a number of years (on the order of 10) and then gradually tapers off until it becomes quiescent, for about 71 per cent of patients who had had their disease 15 years or more stated that it was in remission or was appreciably milder.

Seasonal variations in the severity of the disease were mentioned by 101 of the patients. The seasonal variation was prominent enough in the minds of these patients to cause them to bring it to the attention of the physicians, for neither in the original history taking nor in the follow-up questionnaire was seasonal variation specifically stressed. It is interesting to note that of the 101 patients who noted seasonal change, 78 complained of increased severity during the summer; 10, during the spring; 13, during the winter, and none, in the fall.

Complete leukocyte counts were performed on the peripheral blood in 116 of the patients at the time of examination at the clinic. Eosinophilia was the only consistent deviation from normal. It is seen in figure 2 that the greatest number of patients tested had a low degree of eosinophilia. Eosinophil counts of more than 10 per cent were extremely unusual. The highest recorded eosinophil count was 63 per cent, and this was in a case of moderately severe dermatitis herpetiformis.

There was no relation between the eosinophil level at the time of examination and the duration of the disease. Eosinophil counts were of no value in predicting which patients would have remissions and which would continue to have symptoms.

In general, the severity of the disease at the time that peripheral blood smears were made tended to parallel the degree of eosinophilia; in the mild and moderate forms eosinophil counts were less than 5 per cent, and in the severe forms eosinophil counts were 5 per cent or more. In cases in which more than one eosinophil count was performed, eosinophils tended to be more numerous in the peripheral blood when the disease was most active.

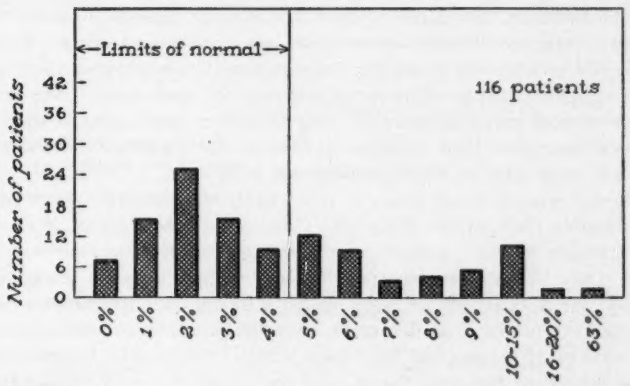

Fig. 2.—Eosinophil count in peripheral blood of patients with dermatitis herpetiformis.

One hundred and twenty-one patients were tested for sensitivity to halogens. Eighty-two were tested for sensitivity to potassium iodide by the patch method. Of these, 50 per cent had a definitely positive reaction. Fifty-two patients were tested by the patch method for sensitivity to potassium bromide, and of these 31 per cent were found to have a positive reaction. Fifty-one persons were given potassium iodide by mouth. Of these, 78 per cent had a definite flare of the dermatitis herpetiformis after small doses of potassium iodide. Four patients had noted a local blistering reaction in areas which had been painted with tincture of iodine. Some patients noted flares of the dermatitis after ingestion of iodine for various reasons.

Some of the patients who were given multiple tests for sensitivity to halogens —for example, patch tests and oral administration of potassium iodide—showed variation in reaction to the various tests. This was apparently a manifestation of the degree of sensitivity to the halogens, for in these persons the positive reaction

was almost invariably to the stronger stimulus; potassium iodide by mouth was the strongest provocation, and the potassium iodide patch test and potassium bromide patch test were weaker stimuli in that order.

There was no discoverable relation between individual sensitivity to halogens, observed in response either to patch testing or to oral ingestion, and the severity or prognosis of the disease. Furthermore, tests of sensitivity to halogens were of limited value as diagnostic tests, merely lending confirmatory evidence when results were positive and meaning little when results were negative.

In our material 119 patients recognized that they had psychogenic factors or were stigmatized as having a large psychogenic factor in their make-up by psychogenic disorders of other body systems. Some of these disorders were hysterical dysphagia, chronic nervous exhaustion, psychoneurosis, functional cardiac neurosis, irritable bowel syndrome, anxiety state, psychopathic personality, chronic ulcerative colitis, neurasthenia and constitutional inferiority. At the time of their first examination 84 of the original 381 patients with dermatitis herpetiformis had conditions which fell into these classifications.

Seventy-four of the 381 patients indicated in their original history or in reply to our questionnaire that flares of their skin disease were intimately related to nervousness, fatigue, overwork or emotional upsets of various kinds. Thirty-nine of the 74 had at least one of the psychogenic disorders mentioned above together with self-recognized flares of dermatitis due to stress and strain. The remaining thirty-five of this group were not among the 84 persons given a diagnosis of psychogenic disorders. Thus a total of 119 out of 381 patients exhibited a definite psychogenic component in their constitutional make-up.

Of the 102 women in our series 11 noted flares of dermatitis herpetiformis just before or during their menstrual period. Three noted exacerbations of their symptoms in relation to the symptoms of the menopause, and one, after an induced abortion. Only four women reported the onset of the disease in association with pregnancy; the disorder of one began within a month after the birth of her child. Two patients reported that dermatitis herpetiformis cleared during pregnancy. Thus a total of 21 women had had exacerbations of dermatitis herpetiformis that might be related to hormonal factors. In the 14 women with premenstrual and menopausal exacerbations and signs, the symptoms conceivably could be related to increased nervous tension.

A "toxic factor" has often been advanced as a cause for dermatitis herpetiformis. In our series only four patients gave a history of flares or onset following acute infections. Several patients noted that after an episode of high fever the skin eruption cleared for a short time. In the period from 1920 to 1930 almost all the patients with dermatitis herpetiformis were investigated thoroughly for foci of infection. Usually a few pus cells in the urine, pyorrhea, alveolar abscesses or bad tonsils were discovered, but rarely did treatment or removal of these foci have any effect on the cutaneous disease. As a matter of fact, five patients indicated that the disease began after tonsillectomy or extraction of teeth.

Systematic allergic surveys were not made on a significant number of these patients, either by specific questioning at the time they were examined or in the questionnaire or by skin testing except by the Hofmeister series of patch tests. Seven patients, however, indicated a belief that the disease was a manifestation of allergy, and the items incriminated ranged from sugar and acids to carbonated water beverages; no two patients named the same items.

We were able to discover only one etiologic factor which was consistent enough in this group with dermatitis herpetiformis to be noted. This was a definite psychogenic factor in roughly a third of the patients in this series.

TREATMENT

In studying the records of this group of patients with dermatitis herpetiformis it was strikingly apparent that until the advent of the sulfonamides, and particularly sulfapyridine, the agents available, with the exception of arsenic, were of little permanent value in controlling the disease. In fact, most of the patients who improved temporarily did so in the hospital, where rest was an outstanding feature of the management of the disease. Most of the severely affected patients were given paravertebral x-ray therapy; six of these reported beneficial effects, one having had a remission for three months followed by a flare and then a permanent remission. Two patients reported relief for six months, and one of them had a permanent spontaneous remission. The remaining three apparently had permanent remissions from the effects of the x-rays; however, these remissions also may

TABLE 2.—*Sequelae of Arsenic Therapy for Dermatitis Herpetiformis*

Form of Arsenic Therapy	Total No. of Patients Receiving Each Form of Therapy	No. of Patients Manifesting Sequelae				
		Keratoses Alone	Pigmentation Alone	Keratoses and Pigmentation	Other Sequelae	Total
Potassium arsenite solution alone	103	11	4	17	1*	33
Asiatic (arsenic trioxide and black pepper) pills alone	81	1	0	3	1†	5
Both Asiatic pills and potassium arsenite solution	24	2	2	3	..	7
Neoarsphenamine	5	0	0	0	..	0
Arsphenamine and potassium arsenite solution	3	0	2	0	..	2
Arsphenamine	1	0	0	0	..	0
Arsenic intramuscularly	1	0	0	0	..	0
Total	218	14	8	23	2	47

* Cirrhosis, multiple neuritis, hepatitis, neuritis (all with keratoses); neuritis alone.
† Neuritis alone.

well have been spontaneous. Of the patients replying and specifying causes of cure or control of their skin trouble, 19 mentioned specific agents exclusive of the sulfonamides and x-rays. Five of these 19 reported that their disorder was controlled by rest or by removal of mental stresses and strains; three reported relief after the administrations of "Chinese herb doctors" and chiropractors; four reported control by local measures, and the remainder said they had been helped by miscellaneous therapeutic agents, such as chaulmoogra oil, married life, liver given intramuscularly, sunlight and spinal anesthesia. These persons probably could be credited with having spontaneous remissions.

Although our study of them ended before the era of the sulfonamides, 16 of the patients of this group later received one of the sulfonamides either specifically for dermatitis herpetiformis or for some acute infection. Of these, one reported an intolerance to the drug and was unable to take enough to determine its effect. Seven received the drug in varying doses, and apparently long-lasting remissions resulted. The remaining eight received the drug and derived benefit from it only

as long as its use was continued. The sulfonamides thus apparently have established themselves as the best agent thus far found for controlling a disease which had resisted therapeutic attack.

Until the advent of the sulfonamides, arsenic in the form of potassium arsenite (Fowler's) solution or as Asiatic pills (arsenic trioxide and black pepper preparation) had been the prime therapeutic weapon. In our group of patients with dermatitis herpetiformis 218 had received varying amounts of arsenic (table 2). It has been a clinical impression that persons with dermatitis herpetiformis tolerate arsenic better than patients having other skin diseases—for example, psoriasis or lichen planus. However, of the 218 patients given arsenic, 47 had arsenical keratoses, pigmentation or other manifestations of arsenism. Of these 47 patients 42 had been given potassium arsenite solution either alone or in combination with other arsenicals. Almost a third (32 per cent) of the 130 patients receiving potassium arsenite solution had signs of chronic arsenic intoxication. Only five of the 81 patients receiving Asiatic pills alone acquired arsenical sequelae; this observation indicates perhaps a lower toxicity of this arsenical preparation. In two patients who had received potassium arsenite solution the arsenical keratoses developed into epithelioma, metastasized and resulted in death. Of the 22 who reported on the present status of their keratoses, 13 still had them in their original intensity as long as 38 years after onset. Five reported that the lesions were better after 14 to 48 years, and two reported that the keratoses had cleared, the condition of one patient in 12 years and the very mild keratosis of the other in three years. Two patients died of arsenical intoxication.

SUMMARY AND CONCLUSIONS

The records of 381 patients seen at the Mayo Clinic during a 20 year period whose condition was diagnosed as dermatitis herpetiformis were examined, and a follow-up questionnaire was sent to each inquiring as to the present status of the disease. It was estimated that in our clinical practice the incidence of this disease was 1 in 500 dermatologic patients examined. Men were found to be affected 2.7 times more frequently than women. It was found that the greatest number of patients with dermatitis herpetiformis first complained of their difficulty in early adulthood although the age at onset ranged from 6 months to 78 years. Through follow-up studies it was apparent that the natural course of the disease was moderate to intense symptoms at the onset and after 10 or more years tapering off of the cutaneous manifestations and perhaps eventual complete disappearance. No relation was found between duration of the symptoms and the original severity of the disease. It was noted by about a fourth of the patients that the symptoms were severest in the summertime. Eosinophilia was the most consistent blood change, and this was of a low order, with counts of more than 10 per cent unusual. Sensitivity to halogens was demonstrated by patients suffering from dermatitis herpetiformis but was not constant enough to be of diagnostic value. In approximately a third of the patients included in our study there was a pronounced psychogenic factor recognized by the patient or by the examining physician.

Treatment until the advent of the sulfonamides had been inadequate or resulted in undesirable sequelae. By use of sulfonamides the disease may be controlled but not cured. One third of the patients receiving potassium arsenite solution were found to have stigmas of chronic arsenism.

ORAL ADMINISTRATION OF PROCAINE WITH ASCORBIC ACID

With Special Reference to the Therapy of Pruritus

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THE IDEA of using procaine hydrochloride for the treatment of allergic conditions is not new. The drug has been used intravenously, with success in many cases, in the treatment of pruritus,[1] status asthmaticus [2] and serum sickness [3] for several years. A recent paper [4] briefly discusses the oral use of a procaine salt in the treatment of bronchial asthma in a person known to be sensitive to the drug when it is given parenterally. This communication is a preliminary report concerning the use of procaine hydrochloride with ascorbic acid by mouth in the treatment of various disorders, many of which have an allergic background.

The pertinent data on 10 cases are presented in the accompanying table. Three representative case records are given below.

REPORT OF CASES

CASE 6.—The patient was a white female nurse, aged 22, who sustained a laceration with a contusion of the left hand from a contaminated instrument. She was given a prophylactic dose (1,500 units) of tetanus antitoxin after a negative skin test reaction had been obtained.

Recovery from the laceration and contusion was essentially uneventful until the ninth day. At that time the patient experienced severe pruritus of the face, neck and shoulders, and particularly at the site of injection of the tetanus antitoxin. A diagnosis of delayed reaction to the antitoxin was made, and the patient was given 50 mg. of tripelennamine (pyribenzamine®) hydrochloride every four hours for 36 hours without improvement. The symptoms became progressively worse, and a weeping, eczematous lesion appeared on the face. Tripelennamine therapy was discontinued, and the patient was given tablets containing a mixture of procaine hydrochloride (300 mg.) and ascorbic acid (150 mg.). Two such tablets [5] were given every four hours for six doses.

The relief of symptoms was dramatic, the pruritus stopping after the second dose. During the ensuing 24 hours the dose was reduced to one tablet every six hours. Forty-eight hours after treatment with the procaine hydrochloride-ascorbic acid combination was started all symptoms had disappeared.

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1. Lundy, J. S.: Clinical Anesthesia; a Manual of Clinical Anesthesiology, Philadelphia, W. B. Saunders Company, 1942, p. 583.

2. Ameville, M. P.: Intravenous Novocaine; Medical Research in France During the War (1939-1945), Paris, Ernest Flammarion, 1947, p. 263.

3. State, D., and Wangensteen, O. H.: Procaine Intravenously in Treatment of Delayed Serum Sickness, J. A. M. A. **130**:990 (April 13) 1946.

4. Schapiro, M. M., and Sadove, M. S.: Oral Procaine Hydrochloride Therapy in Asthma, Ann. Allergy **8**:85 (Jan.-Feb.) 1950.

5. The tablets were supplied as preparation CH-25 by Chilcott Laboratories, Division of the Maltine Company, Morris Plains, N. J.

CASE 8.—The patient was a 55 year old white woman who received 100,000 units of crystalline penicillin G by mouth every four hours (12 doses) for the treatment of an infection of the throat. On the ninth day after penicillin medication was discontinued the patient manifested severe, generalized giant urticaria (one wheal extended from the knee to the greater trocanter and encompassed almost the entire thigh). Pruritus was intense; the patient's oral temperature was 102 F.

Therapy was initiated by giving 750 mg. of procaine hydrochloride and 450 mg. of ascorbic acid (three tablets of CH-25) immediately and two tablets of the combination every two hours for three doses. Thereafter one tablet was given every four hours as circumstances required.

At the end of 18 hours the pruritus had practically ceased. Twenty-four hours after the initiation of therapy some of the wheals were still present, but the pruritus had disappeared and the patient's temperature was normal. At the end of 72 hours the lesions had virtually vanished and the patient was discharged.

Data Concerning Ten Patients Treated with Orally Administered Procaine Preparations

Case No.	Sex	Age	Diagnosis	Therapy	Results and Comments	Side Effects
1	M	48	Atopic dermatitis	Procaine combination A,* 1 tablet four times daily	Pruritus stopped in three days; all lesions clear in three weeks; no recurrence	None
2	F	54	Dermatitis	Procaine combination A,* 1 tablet four times daily	Complete healing in 14 days (incidentally, patient had dramatic relief from rheumatoid arthritis pain, present for three and one-half years); no recurrence	None
3	M	34	Penicillin reaction	Procaine combination A,* 1 tablet every three hours	No relief from previously administered epinephrine; partial relief after third dose of procaine combination; complete healing in 48 hours; no recurrence	None
4	F	4	Food urticaria	Procaine combination A,* ½ to 1 tablet every three to four hours	Relief in 18 hours; no recurrence	None
5	M	32	Intermittent urticaria of unknown cause	Procaine hydrochloride, 300 mg. every three hours	No relief from diphenhydramine and epinephrine; relief in 18 hours after procaine therapy was started; no recurrence	None
6	F	22	Tetanus antitoxin reaction	Procaine-ascorbic acid combination,† 1 to 2 tablets every four to six hours	No relief from tripelennamine; dramatic relief after second dose of procaine-ascorbic acid; cure in 24 hours; no recurrence	None
7	F	22	Contact dermatitis	Procaine-ascorbic acid combination,† 1 tablet four times daily; calamine lotion	Complete relief in 48 hours; no recurrence	None
8	F	55	Penicillin reaction	Procaine-ascorbic acid combination,† 2 tablets every three hours for three doses; 1 tablet every four hours, as required	Subsidence of pruritus in 18 hours; at end of 72 hours almost complete healing; no recurrence	None
9	F	52	Atopic dermatitis	Procaine-ascorbic acid combination,† 1 tablet every four hours	No relief from previous large doses of ascorbic acid, diphenhydramine or tripelennamine; marked exacerbation of symptoms after fourth dose of procaine-ascorbic acid combination; therapy discontinued	Symptoms made worse
10	M	32	Dermatitis	Procaine-ascorbic acid combination,† 3 tablets every four hours	Pruritus and edema relieved in 24 hours; complete clearing in four days	None

* Procaine combination A consisted of procaine hydrochloride, 250 mg.; ephedrine, 10 mg., and methapyrilene, 15 mg.
† The procaine-ascorbic acid combination consisted of procaine hydrochloride, 250 mg., and ascorbic acid, 150 mg.

CASE 10.—The patient, a 32 year old pathologist, had had a vesicular dermatitis of the fingers of both hands. It was at first believed that the lesions were of the venenata variety, but skin tests with formaldehyde solution, xylene, alcohol, cedar oil and other commonly used laboratory agents elicited negative reaction. Pruritus and edema were severe.

Among the medications employed to no avail were methapyrilene (histadyl®) and ephedrine, ascorbic acid, diphenhydramine (benadryl®) and aureomycin. The last-mentioned one was prescribed by a dermatologist on the theory that the lesions were of virus origin. After three weeks the patient was given CH-25 (three tablets every four hours) and all other medication was discontinued. Within 24 hours the pruritus had ceased and the edema was subsiding. Three days later all symptoms had subsided and only a mild erythema remained. It may be of significance that meanwhile the patient continued his duties as a pathologist.

It is of particular interest to note that side effects due to the orally administered procaine-ascorbic acid combination were absent in this trial. This is remarkable in view of the fact that doses of as much as 2,400 mg. of procaine hydrochloride were given daily. Larger doses are now being tried experimentally. The oral toxicity of procaine is probably quite low, preliminary reports [6] indicating that certain animals can tolerate as much as 5 Gm. per kilogram without demonstrable ill effects. Although various drugs were tried in combination with procaine, we are now standardizing on a product containing 250 mg. of procaine hydrochloride and 150 mg. of ascorbic acid per tablet. Better results seem to be obtained with such a combination than with the others which have been used. This observation is in agreement with the findings of Graubard and co-workers,[7] who employed ascorbic acid prior to the intravenous use of procaine. Further work by us and by other investigators is in process.

COMMENTS

Procaine is probably the oldest local anesthetic in general use today, having been introduced into clinical medicine almost 50 years ago. Although a wealth of information has been published about the drug, the great preponderance of reports have concerned the local or parenteral use of the compound. Practically nothing has been found in our search of the literature with respect to the oral use of procaine. The major exception is the paper by Schapiro and associates,[4] who reported the case of a patient with status asthmaticus for whom orally administered procaine was the only medication which afforded any appreciable degree of relief.

In our preliminary study of procaine and ascorbic acid we were a bit skeptical about the initial results, but as our experience has increased we have become more and more convinced that the oral administration of procaine constitutes a completely new approach to the problem of providing relief in certain cases of allergy. The mechanism of action is as yet unknown. It has been speculated that a breakdown product of the digestion of procaine may be responsible for the benefits observed. Further study of this problem is contemplated.

Consideration has been given to the possibility that the ascorbic acid was the primary factor responsible for the remarkable therapeutic effects which have been observed. Although it probably has contributory value, it is doubtful that ascorbic acid exerts the main therapeutic effect, since it has been demonstrated on numerous occasions in the past that when it is orally administered comparatively huge doses (several grams) are necessary for relief of allergic symptoms. Furthermore, these results may be inconsistent, and only when ascorbic acid is given intravenously in 0.5-1.0 Gm. doses repeated several times daily can fairly reproducible results be obtained.

SUMMARY

Procaine hydrochloride in combination with certain drugs, especially ascorbic acid, was given orally to 10 patients with allergic disorders.

The results with the procaine-ascorbic acid combination were highly satisfactory, in some instances superior to those with all forms of medication previously employed.

40 Franklin Street.

6. Dr. William T. Strauss, Medical Director, Chilcott Laboratories: Personal communication to the author.

7. Graubard, D. J.; Robertazzi, R. W., and Peterson, M. C.: Intravenous Procaine; a Preliminary Report, New York J. Med. **47**:2187 (Oct. 15) 1947.

ANTIQUITY OF SYPHILIS WITH SOME OBSERVATIONS ON ITS TREATMENT THROUGH THE AGES

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FOR MANY years one of the interesting subjects in medical history has been the origin of syphilis, which disease was indelibly brought to the attention of the then civilized world at least as early as the late fifteenth century. The advent of printing no doubt had something to do with the world's first knowledge of the disease. From that time on we have very authentic reports in regard to its spread. A question that has further arisen is, how much was known of this disease or how much was written in regard to it before this date? Was this a condition that had come down through history along with the many other plagues that have affected the human race, or is it actually true that syphilis was brought to the civilized world by Columbus and his sailors when they returned from Hispaniola? Consideration of these problems has given rise to a discussion that has been going merrily on not only for decades but even for several centuries. Whether the question will ever be definitely settled is hard to say; that it will always be a subject of interest is undeniable. No doubt, in the future, as in the past, sides will be taken and each side will have its proponents. For example, the German medical historian Sudhoff [1] has constantly fought the idea that syphilis was transported from America. He has found in the Copenhagen Library prescription books for the "mal Franzoso" which date back to the first half of the fifteenth century and have been expertly authenticated as to age. In his stand he takes the part of the great Viennese medical historian, Prof. J. K. Proksch,[2] who says, "There is no question but that syphilis was present in antiquity even though it was not recognized by the physicians" and,[3] "Hensler, who spent more than twenty years on the study of the sources of the history of syphilis and on related external diseases, concludes that syphilis, under the form of herpes of the Greeks and formica of the Arabians, has existed since the memory of man throughout the entire Dark Ages."

Read at the William Allen Pusey Memorial Dinner, Chicago, Oct. 18, 1950.

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1. Sudhoff, K. F. H.: Mal franzoso in Italien in der ersten Hälfte des 15. Jahrhunderts, in Sudhoff, K. F. H., and Sticker, G.: Zur historischen Biologie der Krankheitserreger, Giessen, A. Töpelmann, 1912, no. 5. Graphische und typographische Erstlinge der Syphilisliteratur aus den Jahren 1495 und 1496, Munich, C. Kuhn, 1912; Amerikanischer Ursprung und Mal franzoso um die Mitte des 15. Jahrhunderts in Italien, Dermat. Ztschr. **20**:325-330, 1913.

2. Proksch, J. K.: Die Geschichte der venerischen Krankheiten; Eine Studie, Bonn, P. Hanstein, 1895-1900, vol. 1.

3. Proksch,[2] p. 275.

On the other hand, Prof. Iwan Bloch [4] of Germany thinks all available statements and facts point to the last decade of the fifteenth century, particularly the years 1493 to 1500, as the time when syphilis first appeared in the Old World. He says there is not a particle of evidence to show that the disease existed in Europe before that time. He thinks it was brought to Europe by Columbus' sailors. Bloch argues that the literature of the Old World before 1495 gives no description of the syphilitic syndrome. He says Virchow has repeatedly declared that there are no pre-Columbian bones with syphilitic change. In his opinion the spread of syphilis followed the campaign of Charles VIII of France down into Italy in 1494-1495. He thinks the malignity of the disease of that time is further evidence of its implantation on fresh soil. He also bases his opinion on the authentic reports of the Spanish authors Díaz de Isla, Oviedo and Las Casas.

However, to quote Lancereaux [5]:

> Observations made at the end of the eighteenth century and commencement of the nineteenth prove, in fact, that syphilis was unknown, or at least very little spread in the north and south of America, so long as the natives remained separated from the Europeans, but that afterwards the extension of that disease was always proportional to the intimacy of the relations established between them.

Prof. C. H. Fuchs [6] of Jena for a long time adhered to the concept of the Columbian origin of the disease but later became a firm believer in its antiquity in Europe. He decided that the conditions described by the Arabians as formica, saphati or assaphati, or as anthimati and elephantiasis by the Greeks, were many times syphilis. He says, "Of a transatlantic American origin one finds not even a syllable among German publications."

In this country, our old friend and revered member, William Allen Pusey,[7] with Sir William Osler,[8] among others, believed in the American origin of syphilis.

Proksch, during his lifetime, probably had the largest library devoted to venereal diseases that had ever been assembled. He felt that syphilis was probably described in the writings of the ancient inhabitants of India, likewise by the Babylonians, and possibly by the Israelites. He said that many medical men have felt that the leprosy of the ancients was not always lepra vera but rather was often lepra spuria, i. e., syphilis. Is it possible that the physicians of Greece and Rome really dealt with syphilis but did not recognize it? Hippocrates,[9] in 460 B.C., described ulcers on the head, accompanied with spots on the back, the genitalia and the uterus. He also described caries (syphilitic?) of the hard palate. Rufus of Ephesus (A.D. 100) understood the relationship between genital sores and bubos and described "thymus," a "spongy hypertrophied flesh,"

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4. Bloch, I.: Der Ursprung der Syphilis; eine medizinische und kulturgeschichtliche Untersuchung, Jena, G. Fischer, 1901, vol. 1, pt. 1.

5. Lancereaux, E.: A Treatise on Syphilis; Historical and Practical, translated by G. Whitley, London, New Sydenham Society, 1868-1869, vol. 1, p. 57.

6. Fuchs, C. H.: Die ältesten Schriftsteller über die Lustseuche in Deutschland, von 1495 bis 1510, nebst mehreren Anecdotis späterer Zeit, gesammelt und mit literarhistorischen Notizen und einer kurzen Darstellung der epidemischen Syphilis in Deutschland herausgegeben, Göttingen, Dieterich, 1843.

7. Pusey, W. A.: The History and Epidemiology of Syphilis; The Gehrmann Lectures, University of Illinois, 1933, Springfield, Ill., Charles C Thomas, Publisher, 1933.

8. Osler, W.: Fracastorius, Proc. Charaka Club **2**:5-20, 1906.

9. Cited by Proksch,[2] p. 128.

which came on the anal area, genitalia and other parts of the body. He stated that some thymi were mild and healed of themselves,[10] while others were incurable. Proksch [2] and Lancereaux [11] thought that the morbus campanus of Horace's satires was syphilis. Tacitus [12] and Suetonius [13] tell us that Tiberius suffered from a disease in which he lost his hair and had his face covered with ulcers and usually with plasters. In many of the early medical writings comments are made concerning boils on the genitalia and also warts appearing on the genitalia and around the anus. Whether these were the type of excresences that we now know to be due to syphilis is, of course, hard to say. The Arabians, though perhaps recognizing a generalized disorder in connection with sores on the genitalia, were not any surer of their ground than either the Greeks or the Romans. Two of the great physicians of antiquity, Galen [14] (A.D. 131) and Celsus [14] (125 B.C.), both speak of ulcerations of the genitals and of ulcerations of the mouth and nose but do not connect them. They, of course, both recognized gonorrhea; in fact, this disease has been known since the time of the ancient Egyptians. Western medicine is indebted to the Arabians for the introduction of mercury compounds from India. One of the physicians of the Dark Ages, Alexander of Tralles,[15] recommended a form of mercury, cinnabar, in a preparation containing 28 ingredients, for chronic swelling of the lymph nodes and wartlike sores on the genitalia and around the anus.

Fuchs [6] translated Nicolaus Myrepsos' medical formulary.[16] This celebrated physician worked in the thirteenth century. He recommended the rubbing in of mercury ointment for ulcers of the tonsils and gums, for putrescence, noma and carbuncles of the genital regions. It is thought by some that the words "malum mortuum," as used by ancient physicians—among others, John of Gaddesen, Lanfranchi, and Gordon—probably constituted the term for syphilis. In fact, later, the celebrated John DeVigo, who worked in the first part of the sixteenth century and published a book on surgery in 1514, said that this disease was like morbus gallicus. His book on surgery was very popular and went through 54 editions. We find that Theodorich of Cervia [17] in the thirteenth century recommended the rubbing in of a mercury ointment for the beginning stage of lepra as an "experimentum infallibile." Was the disease true leprosy, or was it perhaps syphilis? Proksch [18] writes the following account:

> Nikolaus von Kurnik, Bishop of Posen, died in March, 1382; he associated with whores and received a chancre "morbus cancri" on the genitalia, sores on the tongue and in the throat, with such ulceration that he could hardly speak. There was a profuse discharge from his mouth, which he could hardly close. The right side of his body was also affected.

Johannes Baptista Fulgosus,[19] Doge of Venice from 1478 to 1483, wrote that two years before Charles VIII of France came to Italy on his campaign to Naples

10. Cited by Proksch,[2] p. 135.
11. Lancereaux,[5] p. 58.
12. Cited by Proksch,[2] p. 202.
13. Cited by Proksch,[2] p. 203.
14. Cited by Proksch,[2] p. 203.
15. Cited by Proksch,[2] p. 153.
16. Proksch,[2] p. 408.
17. Cited by Proksch,[2] p. 411.
18. Proksch,[2] p. 364.
19. Cited by Proksch,[2] p. 317.

they had a new disease in Venice which they called the Neapolitan disease, the Gallic disease or St. Job's disease. After intercourse the patients had a sore on the genitalia, then pain in the limbs and ulcers on the body. Fulgosus declared the disease came to Italy from Spain out of Ethiopia. His account was corroborated by Senaregga, the Genoese ambassador, who claimed the disease was in Italy before the campaign of Charles VIII and began with genital lesions, pains in the limbs and ulcers on the body. He compared the disease to lepra. Fatal cases were rare, and in the lowest types of society few remained free from it. Even these early physicians had certain ideas in regard to prevention of disease; for example, we find the celebrated medical school of Salerno, as early as 1300, advising washing of the genitalia and immediate urination after coitus.

A priest, Michael Scotus,[20] in 1477 wrote an article saying that a young man who slept with a woman having a discharge contracted lepra and, further, that if conception took place one or more diseased creatures would be born. Was leprosy or syphilis meant? Conrad Schellig,[21] personal physician to Phillip von der Pfalz, in 1499 wrote of the "mal de franzosen" that to him was not a new disease but the well known formica. Widmann,[22] in 1501, writing about the pestilence, wrote that the "mal de franzosen" and formica and saphati of the Arabians were the same.

Feodorico Borgognoni [23] (1205-1298) was a physician in Bologna and after 1266 was Bishop of Cervia. His book on surgery was finished in 1266 and contained the first descriptions of methodical inunction with mercury salve. The inunctions were recommended for scabies, cancer, malum mortuum and leprosy. The rubs were considered beneficial only in the beginning stages of leprosy. Borgognoni preferred the so-called Saracen salve.

Francisco de Villalobos,[24] a Spanish author, in 1498 wrote a book concerning the "pestiferous bubas" (syphilis) and stated that the disorder was like the sarna of Egypt, which dated back to Biblical times.

Proksch believes that syphilis was well recognized among the laity hundreds of years before Columbus discovered America. He makes the significant point that up to about 1495 leprosy had been one of the worst scourges of the human race and that malum mortuum, ignis persicus, asaphati, elephantiasis and formica had also been severe afflictions. Yet after this time, leprosy almost died out—in fact, today we find very little leprosy in Western Europe—and malum mortuum, ignis persicus, asaphati, elephantiasis and formica also disappeared. How can this occurrence be explained except on the basis that syphilis was the disease the patients had?

To clarify the confusion between syphilis and leprosy, Holcomb,[25] a captain in the Navy and a gifted litterateur, says that ancient leprosy, so-called, was always regarded as a readily contagious disease and spread through contact with a

20. Cited by Proksch,[2] p. 362.

21. Cited by Proksch,[2] pt. 1, p. 27.

22. Cited by Proksch, [2] pt. 2, p. 20.

23. Cited by Proksch,[2] p. 291.

24. de Villalobos, F. L.: El sumario de la medicina, con un tratado sobre las pestíferas bubas, Salamanca, 1498.

25. Holcomb, R. C.: Christopher Columbus, and the American Origin of Syphilis, U. S. Nav. M. Bull. **32**:401-430 (Oct.) 1934; Antiquity of Congenital Syphilis, Bull. Hist. Med. **10**:148-177 (July) 1941.

menstruous woman (Bartholomeus Anglicus, Peter Abano, Peter Angelata). Holcomb says Mathew of Paris estimated that the leper houses had grown since the Crusades until there were 19,000 of them. They were all abolished by the Bulls of Pope Innocent VIII of 1490 and of Pope Julius II of 1505, and the Order of St. Lazarus was no more; on the other hand, syphilis increased in the same proportion.

Likewise, Haberling, Professor of the History of Medicine in Düsseldorf, points out that according to the researches of Sticker, along with the term "lepra vera," again and again one finds in the writings of the physicians of the Middle Ages the expression "lepra spuria," applied to a disease which, in contradistinction to lepra vera, did not require isolation and was curable.[26] This "lepra spuria," to which, in the course of time, many other names were assigned, was doubtless syphilis brought in from the Orient by persons returning from the Crusades.

Documents on the history of syphilis have long circulated in Paris. These contained laws of Parliament and orders of the provost of Paris in respect to official measures against the "grosse vérole." Astruc, who believed in the Columbian origin of syphilis, published such a document of June 25, 1498, after Columbus's discovery of America; however, Proksch [27] tells us that Galligo found one of these documents and reported it dated March 25, 1493. It required all persons sick with the "grosse vérole" to live out of the city under penalty of being tossed in the river. And as to Columbus and the New World origin of the disease, his ships the Pinta and the Nina did not reach Palos until March 15, 1493.

Thomas of Gascoigne, Chancellor of Oxford, preserved at Lincoln College in Oxford an old document in which he described the disease of John of Gaunt, Duke of Lancaster. John of Gaunt on his death bed related to King Richard II that his throat trouble, putrified genitalia and sores on the body were due to dissoluteness with whores. Richard related this to a man of whose account Thomas of Gascoigne made a written copy in 1430. This manuscript was found by William Wagstaffe, and it was published in *Philosophical Transactions* (London) by William Beckett.[28]

Heinrich Von Pfolspeundt [29] in 1460 wrote a book in which were described "wilde Wärtzen" (wild warts), which were found not only on the genitalia and anal area but all over the body. For treatment he suggested mercury salve. Johannes Grünpeck,[30] himself a patient, gave his book published in 1496 the title "Ein hübscher Tractat von dem Ursprung das bösen Franzos, das man nennet die wylden Wärtzen." Moreover, Sebastion Brant [31] prayed to St. Fiacrino in 1496 that young men be protected from the "schweren kranckheit der blätern und wärtzen." He said only grace from heaven, patience, Mithridates (mercury) pills and frequent blood letting would help.

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26. The Discovery of Syphilis, Foreign Letters (Berlin), J. A. M. A. **105**:2172 (Dec. 28) 1935.

27. Proksch,[2] pt. 3, p. 344.

28. Beckett, W.: A Letter Concerning the Antiquity of the Venereal Disease, Phil. Tr. Lond. **31**:47-65, 1720.

29. Cited by Proksch,[2] p. 354.

30. Grünpeck de Burckhausen, J.: Ein hübscher Tractat von dem Ursprung des bösen Franzos, das man nennet die wylden Wärtzen; Auch ein Regiment wie man sich regiren soll in diser Zeyt, Augsburg, 1496.

31. Cited by Proksch,[2] pt. 1, p. 155.

Pedro Pintor [32] practiced in Spain up to 1494 and was then personal physician to Pope Alexander VI and some of the Borgias. He published a book of the greatest rarity in 1500 and stated that the disease had been in Rome since 1494 but that he had previously seen it in Spain. Pintor thought it was like the aluhumata of the Arabians. He was acquainted with its different forms and chronicity and differentiated between the mercurial and syphilitic change found in the mouth.

Torella [33] practiced in Spain up to 1493 and was then personal physician to Rodrigo de Borgia, later Pope Alexander VI. His clientele was restricted to the papal court, including the pope, and yet in September and October 1497 he successfully treated 17 cases of the disease and described the course of the separate cases in his book. The notorious roué and son of the pope, Cesare Borgia, one of the patients, was made cardinal in 1492 at the age of 15. Torella speaks of him as reverendissimus et illustrissimus in Christo pater.

In our opinion these reports and extracts go far in showing that long before the end of the fifteenth century there was a venereal disease found throughout the Far East, the Egyptian, Grecian and Roman Empires and Europe in general which was variously called leprosy, leprosy spuria, aluhumata, sarna, maluum mortuum, saphati, asaphati, Blättern, wilde Wärtzen, mal Franzose, mentagra, grande vèrole, gore, grande gore, pustulis, elephantiasis, bubas, grosse vèrole, grosse Blätter, scorra pestilentialis, pudendagra, mal de Naples, great pockkes and disease of St. Minus, of St. Sementio, of St. Roche, of St. Sebastian, of St. Evagius and of St. Job. Holcomb [25] gives the number of different names as around 600, from carrott of Iceland to yeng-men chang of China. And in 1530 Fracastorius [34] wrote his celebrated poem "Syphilis, sive morbus gallicus." The name Syphilis was that of a shepherd sick of a disease, nonvenereal in type, which had been inflicted on him by a sun god whom he had cursed for killing his sheep, who first used guaiacum, a remedy revealed by a goddess. Sir William Osler says this is the best known medical poem ever written.

Ulrich von Hutten (1488-1523), knight, a follower and great friend of Martin Luther, contracted syphilis at an early age. Hutten says [35] that the physicians have, out of disgust for the hateful, filthy disease, turned over its care to a group of barber surgeons and bunglers, of which Grünpeck as a patient also complained. Hutten says they first planned on burning out the condition by corrosive medicaments, but since it was not possible to touch all the ulcers they would have had these healed by a salve to which mercury was added. He elaborates at great length in his book on the mercury treatment of the disease, on mercurial poisoning, from which he suffered for nine years, and on his final cure following the use of guaiac. His book was published in 1519, but the "cure" apparently did not last, for he was dead in 1523. There were four editions of his work—all of them very scarce—within a few years.

It was the books of von Hutten that were probably among the first to call the attention of Europe to the drug guaiac. Guaiac was used first in Spain, and

32. Cited by Proksch,[2] pt. 1, p. 28.

33. Torella, G.: Tractatus cum consiliis contra pudendagram, sive morbus gallicum, Rome, 1497.

34. Fracastorius, H.: Syphilis, sive morbus gallicus, Verona, S. Niccolini da Sabbio, 1530.

35. von Hutten, U.: De guaiaci medicina et morbo gallico liber unus, J. Scheffer, Mainz, 1519.

knowledge of its use spread very rapidly over western Europe. The physicians and barber surgeons very soon were divided into two schools—those that stood by mercury for treating syphilis and those that used "the woods." Some used both.

We might go on endlessly giving the viewpoint as to the respective values of mercury, guaiac and other remedies. The physicians' prescriptions were always very intricate and usually secret. The greater the number of constituents, including angleworms, the greater the potency was supposed to be. The use of guaiac, however, brings us to another chapter of the story—the theory of the New World origin of syphilis.

The belief in the Columbian, or New World, origin of syphilis has gained a large number of followers, thanks to the publications of Gonzalo Fernandez Oviedo y Valdes,[36] Ruy Díaz de Isla,[37] Francesco Delicado, or Delgado,[38] and Montejo y Robledo,[39] as well as those of Astruc,[40] Herman Boerhaave's Luisini [41] and, more recently, Bloch.[4] In this country these claims have been accepted by the late William Allen Pusey,[7] Sir William Osler [8] and others. Moreover, Herbert U. Williams,[42] in a very scholarly and thorough investigation, has attempted to solve the problem by a careful examination of bones in ancient burying mounds, cemeteries, and the like.

And, too, Hiram Bingham,[43] in his latest volume, "Lost City of the Incas," giving an account of the culmination of his explorations around Machu Picchu, claims that the pre-Columbian Incas show plenty of evidence of syphilis in their bones. Bingham does admit that in certain instances earlier burials had been disturbed to make room for later ones, in an old trick of the grave digger. In the instance of the bones of the Mama Cuna, or Mother Superior, of the Virgins of the Sun, this practice may not have been employed, and yet examination of the

36. de Oviedo y Valdes, G. F.: De la natural historia de las Indias, Toledo, 1526; La historia natural y general de las Indias, Seville, 1535, pt. 1.

37. Díaz de Isla: Tratado contra el mal serpentino: que vulgarmente en Espana es llamado bubas que fué ordenado en el ospital de todos los santos de Lisbona, Seville, 1539.

38. Delgado, F.: Del modo di adoperare el legno santo, di India occidentale, salutifero remedio ad ogni piaga; Del modo di adoperare el legno santo, ovrero del modo de guarire il mal Francese ed ogni mal incurabile, Venice, 1529.

39. Montejo y Robledo: ¿Cuáles son las principales enfermedades contagiosas qui recipro-camente han cambiado entre si los pueblos del Antiguo y del Nuevo Mundo? (Procedencia americana de las Bubas), in Fourth International Congress of Americanists, Madrid, 1883-1884, vol. 1, p. 331.

40. Astruc. J.: De morbis venereis libri novem, revised ed., Paris, 1740.

41. Luisini, L.: Aphrodisiacus, sive de lue venerea; in duos tomos bipartitus, continens omnia guæcumque haetenus de hac re sunt ab omnibus medicis conscripta; Ubi de ligno Indico, salsa perilla radice chynae, argento vivo, caeterisque rebus omnibus ad hujus luis proflegationem inventis, difusissima tractatio habetur, corrected and revised ed., Lyons, J. A. Langerak and J. and H. Verbeek, 1728 (Preface by Hermann Boerhaave).

42. Williams, H. U.: The Origin and Antiquity of Syphilis: The Evidence from Diseased Bones; Review, with Some New Material from America, Arch. Path. **13**:779-814 (May); 931-983 (June) 1932.

43. Bingham, H.: Lost City of the Incas; The Story of Machu Picchu and Its Builders, New York, Duell, Sloan & Pearce, Inc., 1948.

skeleton showed that the woman had had syphilis. The osseous material found was returned to New Haven and has been examined by Dr. George F. Eaton,[44] who corroborated Bingham's observations.

It is Williams' feeling that there is plenty of pre-Columbian osseous material in America showing evidence of syphilis and that there is no such acceptable evidence from European or Asiatic material. To this, Holcomb [45] replies that Dr. Ales Hrdlicka considers that those American burying places which show syphilitic bones also give sure evidence of being post-Columbian. Holcomb also asks, how explain aneurysms, which were well known to Galen and Celsus in Roman times? Holcomb says that the Latin translation of Ruy Díaz de Isla made by George Jerome Welch in 1688 was the only part of the work known to Astruc and many other writers, including Hermann Boerhaave, who were the first Europeans to take up the cudgel for the Columbian origin of syphilis. Williams [46] has more recently further taken up the cudgel for it through the help of a Nicaraguan scholar and John P. Rice, professor of Romance languages at the University of Buffalo. They examined the original sources of Oviedo, Las Casas and Díaz de Isla and on the basis of the data found strongly favored the idea of the New World origin of syphilis.

Holcomb [25] tells us that John Manard (1462-1536) in 1525 wrote Michael Sanatannam a letter, published in Venice, in which the disease is said to have been encountered in newly discovered countries and then spread by the army of Charles VIII of France while it was in Italy. Bloch takes his Columbian stand on the basis of this letter and on the writings of Ruy Díaz de Isla.[37] Díaz de Isla claimed that Spaniards infected in the New World with the new disease brought it back to Spain and soldiers thus infected were either in Charles VIII's army when it invaded Italy or were with the army defending Naples against Charles's forces. As to Charles VIII, he entered Naples on Feb. 22, 1495, without opposition and left there May 20, 1495. The Spanish relief forces never entered there until after Charles had left. From various accounts it is probable that Charles's men were troubled with typhoid, typhus and syphilis, but the syphilis was not contracted from the Spaniards. Charles's army took 1,000 prostitutes with them when they invaded Italy and probably picked up many more in their stops at Florence, Rome, etc. He and his army did not get back to Grenoble until Oct. 27, 1495, and, as Holcomb [25] notes, Kaiser Maximilian's blasphemy edict at the Diet of Worms on account of the scourge of syphilis was dated a month and 20 days earlier. This account shows conclusively that the disease was already quite prevalent throughout Germany. No, the sailors of Columbus did not bring the new disease from Spain to Italy, as is claimed by Díaz de Isla, Oviedo and las Casas. It was already there. Moreover, Morison,[47] in his recent carefully documented "Life of Columbus," tells us that Columbus kept daily health reports in his journals which are still available and for his first two voyages there is a strange silence from him and from Dr.

44. Eaton, G. F.: The Collection of Osteological Material from Machu Picchu, in Memoirs, New Haven, Yale University Press, 1916, vol. 5.

45. Holcomb, R. C.: Who Gave the World Syphilis? The Haitian Myth, New York, Froben Press, Inc., 1937.

46. Williams, H. U.: American Origin of Syphilis, with Citations from Early Spanish Authors Collected by Dr. Montejo y Robledo, Arch. Dermat. & Syph. **16**:683-696 (Dec.) 1927.

47. Morison, S. E.: The Sinister Shepherd, in Admiral of the Ocean Sea; a Life of Christopher Columbus, Boston, Little, Brown & Company, 1942, vols. 1 and 2, chap. 37.

Chanca, the physician on the second fleet, with regard to any illness. The earliest record of an outbreak of syphilis among the Europeans in Hispaniola is that of Ferdinand Columbus, in his account of the third voyage, who says his father, on arriving at Santo Domingo on Aug. 20, 1498, found the island in great tumult because a large part of the people left there were dead and 160 of the others had bubas (syphilis). This occurrence was after at least three great fleets had brought Spanish immigrants to Hispaniola in 1495-1496, and it was the acknowledged custom for all Spaniards landing in the New World to claim four virgins as wives. (The Carib chieftain thought two would be ample, according to Holcomb.) Las Casas [48] and Oviedo (cited by Holcomb [25]) tell us that there were two diseases in the Indies dangerous to the Spaniards, the bubas and chiggers, and that the natives had the former in a milder form but that it was very severe in its effects on the Spaniards.

Lastly, it is strange that, if syphilis was brought to Europe from the New World, these claims were not made until almost a generation after its discovery and the first Spanish authors writing about the disease all believed in the antiquity of bubas, as they had called it for years and years. Villalobos,[24] Almenar,[49] Torella [33] and Pintor,[50] all writing around or not later than 1500, thought the disease was like the ancient sarna of Egypt. Pintor compared it to the aluhumata of the Arabians. Even Ruy Díaz de Isla, whose book on "the serpentine disease" appeared in 1539 and who was not a physician but a barber surgeon, although in one place claiming a New World origin for the condition, in another compares it to the "mentagra" of Pliny and to the ancient "empeynes" of Spain.

Oviedo, in his large work on the Indies, attempts to justify the Spaniards' terrible treatment of the natives. He does not think, however, that an effort at justification is the reason certain Spanish authorities claimed that syphilis was contracted from the New World. On the other hand, many writers adopt that very view and also point out that it was most convenient along with this line of argument to bring forth the remarkable cure for the disease, guaiac, that was ostensibly already on the ground. Oviedo claimed that its being there was God's providence. At any rate, it turned out to be for Spain a veritable gold mine, thanks especially to the book of von Hutten and to that of Nicholas Poll and others.

Poll's tract [51] on the guaiac treatment of syphilis was printed at Venice in 1535. However, according to Fisch,[52] Poll's tractate was dated Dec. 19, 1517, although not published until 1535. It was addressed to Matthew Lang, Cardinal of Gurk and Bishop Coadjutor of Salzburg. Poll had the position of professor of medicine and also that of physician to His Imperial Majesty Maximilian, the author of the blasphemy edict. It is probable that Poll and Paulus Ricius were sent to Spain at the considerable expense of Cardinal Lang, or perhaps of the Fuggers of Augsburg,

48. Las Casas, B.: Historia de las Indias, Marqués de la Fuensanta del Valle and Don José Sancho Rayón, 1875-1876, vol. 5, p. 233.

49. Almenar, J., and Nicolaus, L.: De morbo Gallico, Lyons, 1529.

50. Pintor, P.: Aggregator sententiarum doctorum omnium de praeservation et curation que pestilentiae, Rome, 1499.

51. Poll, N.: De cura morbi gallici per lignum guaycanum, libellus, Venice, G. Padovano and V. Ruffinelli, 1535.

52. Fisch, M. H.: Nicolaus Pol Doctor 1494; with a Critical Text of His Guaiac Tract Edited with a Translation by Dorothy M. Schullian, New York, Herbert Reichner, 1947.

to study the new guaiac treatment of syphilis. Moreover, this same Ricius, as Fisch shows, was the one who gave the guaiac treatment to Ulrich von Hutten, famous for his tract on guaiac treatment of syphilis, dated 1519. Fisch thinks it probable that the cardinal had more than an altruistic motive in this journey, i. e., his own health.[53] Within a year after Poll's tractate was written, Schmaus [54] published a pamphlet on the guaiac treatment which was printed in Augsburg and there was an anonymous pamphlet on the same subject, entitled "A Recipe for Using a Wood for the French Disease and Other Running Sores," translated from Spanish into German. Fisch says that the latter was the first published recipe. De Isla, in his book written in 1539, notes that in 1504 he received a written account of the use of guaiac. But there are no authentic proofs for these statements. Hutten makes the statement in his book that the remedy was found in the preceding two years, i. e., around 1516. Hutten tells us, according to Fisch, that a Spanish governor afflicted with syphilis was shown the guaiac treatment by the natives. Later this governor was identified with Gonzalo Fernandez de Oviedo. Oviedo went to the Indies in April 1514 and returned in December 1515. However, his books were not published until 1526 and 1535. Fisch thinks it is possible that the wood was first imported and used around 1516. He cites Wilhelm Rem, in his Augsburg chronicle, as saying that the wood was first brought to Augsburg from Lisbon in 1518 and sold at 3 florins a hundred. Drinking the decoction cured the pox in 30 days, and 30,000 were said to have been healed in Spain—conservative Poll put the number at 3,000. The Fuggers, celebrated merchants of Augsburg, did a big business, and in their model housing center, the Fuggerei for people in moderate circumstances, three units were devoted to the syphilis hospital, which was called the Poxhouse or the Woodhouse.[52] Paracelsus scoffed at this treatment—to his credit he stood by mercury therapy even though his technique of semisecretiveness and semicharlatanism was not admirable (though characteristic of the age). Massa reports that at Venice guaiac on its first appearance sold for 50 crowns an ounce, a price which made some, after they had made use of them, sell the chips again and again to the apothecary, who in the same manner sold it 10 times over.[52]

Here was a remedy that was better than gold. The king of Spain ordered that a substantial part of each ship's cargo returned to Spain be guaiac wood. It is not too difficult to see that this emphasis on the origin of syphilis in the Indies and on guaiac as the cure of syphilis may have been a "put up job." Professor Haberling of Düsseldorf, a medical historian of note, takes this stand.[26] He does not see how the theory of the Columbian origin of syphilis can be taken seriously, and he thinks the fable was linked up to the growing trade in guaiacum wood. He also thinks reports of the devastating epidemic of syphilis in Naples and Germany were pure fabrication.

However, many a remedy that has bloomed for a day begins to wane when its true value is found, and Lancereaux tells us that as early as 1546 Fracastorius, who gave syphilis its name, asserted that the wood should be used in stronger doses and for a longer time. Does this advice sound familiar? Use of guaiac gradually fell into discredit. Cinchona was introduced and used by Emperor Charles V.[5] Then

53. Fisch,[52] p. 39.

54. Schmaus, L.: Lucubratiuncula de morbo gallico et cura ejus noviter repeta cum ligno indico, Augsburg and Marc Wyrsung, Sigismund Grimm, 1518.

sarsaparilla and sassafras [55] were tried out. In fact, sassafras acquired a high repute and a high price was commanded for the root. Sir Walter Raleigh held the patent for the whole of the north part of Virginia (at that time containing New England). Moore and Manning tell us that Goswold in 1602 and Pring in 1603, under the patronage of the Earl of Southhampton, brought back from Cape Cod to London enough of the root to cause a considerable drop in the regular price of 20 shillings a pound. Raleigh sought compensation, but Southhampton's influence protected Goswold and Pring.

But we are getting away from our main subject. Did syphilis originate in the Americas, or was it already prevalent in Europe before the discovery of the New World?

It is believed enough authorities have been cited to show that syphilis under various names was well recognized and treated with mercury in various forms long before the discovery of America. On the other hand, if we are to accept Williams's studies on bones and Bingham's investigations in Peru, there is a possibility that syphilis was also prevalent in the Americas before Columbus touched our shores. After all, the New Hemisphere was probably peopled with explorers by way of the Bering Straits. And syphilis is certainly an old disease in the Old World. Lancereaux, Holcomb and Hrdlicka all make the statement, not in exactly the same words, that the introduction of syphilis among the natives in America depended on the recent proximity of the white man, and this may well be true.

I doubt that this debatable problem will ever be solved to the satisfaction of all.

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55. Moore, M., and Manning, C.: Syphilis and Sassafras; Information Relating to "Plant of Sovereigne Vertue for French Pox" and Early Voyages to New England, Am. J. Syph. **20**:646-650 (Nov.) 1936.

MELANIN PIGMENTATION AND HEPATIC DISEASE

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HEPATIC disease manifests itself not infrequently by producing changes in the skin, changes which include such well known phenomena as the sudden appearance of spider nevi, palmar erythema and gynecomastia. A considerable body of evidence exists suggesting that these changes are produced by the local action of circulating estrogens which the liver, in its damaged state, is unable to inactivate. Alternatively, these changes may occur in the presence of a healthy liver when the level of circulating estrogen is higher than that with which the liver is normally capable of dealing. Bean and his colleagues (1949)[1] have recently described the appearance of palmar erythema and spider nevi in pregnant women, while the gynecomastia of puberty is thought to be due to a sudden increase of circulating estrogen which upsets the normal estrogen-androgen balance. Gynecomastia has also been described as occurring under conditions following starvation, by Jacobs (1948),[2] and in cases of cirrhosis of the liver, by Glass and his associates (1940).[3] The mechanism is discussed in each case, and it seems likely that the estrogen-detoxicating metabolism is at fault.

Increased melanin pigmentation associated with hepatic disease has not been described previously except by Osler, who mentions a "bronzing" of the skin in some cases of Hanot's biliary cirrhosis. Certainly the condition is not discussed by Wiener (1947),[4] who summarizes most of the cutaneous manifestations of liver damage. Acanthosis nigricans, a condition characterized by roughening and darkening of the skin and associated in 50 per cent of cases with carcinoma (Curth, 1948),[5] has not previously been considered due to involvement of the liver. This possibility will be discussed after a description of some clinical cases of increased pigmentation.

REPORT OF CASES

CASE 1.—A woman aged 53 was first seen in 1945, when she was found to be jaundiced and deeply pigmented. She also had an enlarged, irregular, firm and painless liver. She was considered to have a case of hemochromatosis. In April 1947 she was again admitted to the hospital, at which time she complained of pain in the groins associated with fever. She was

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1. Bean, W. B.; Cogswell, R.; Dexter, M., and Embick, J. F.: Surg., Gynec. & Obst. **88**:739, 1949.

2. Jacobs, E. C.: Ann. Int. Med. **28**:792, 1948.

3. Glass, S. J.; Edmondson, H. A., and Soll, S. N.: Endocrinology **27**:749, 1940.

4. Wiener, K.: Skin Manifestations of Internal Disorders (Dermadromes), St. Louis, C. V. Mosby Company, 1947.

5. Curth, H. O.: Acanthosis Nigricans and Its Association with Cancer, Arch. Dermat. & Syph. **57**:158 (Feb.) 1948.

still deeply jaundiced and showed pronounced brownish gray pigmentation, most noticeable in the folds and flexures of the skin and around the eyes. The clinical condition of her liver had not altered greatly over the preceding two years. The patient was seriously ill and died shortly after admission. At autopsy she was found to have osteomyelitis of the pubic symphysis, toxic myocarditis and multilobular cirrhosis of the liver. The cut surface of the liver failed to give a positive prussian blue reaction, and a piece of skin removed from the axilla showed heavy melanin pigmentation in the basal layers but no free iron. The histologic picture of the liver was that of multilobular cirrhosis and showed considerable deposits of pigment in the cells. The adrenal glands were normal. The diagnosis of hemochromatosis was revised, and it was thought possible that the patient's pigmentation was secondary to the liver disease.

CASE 2.—A man aged 62 was admitted to the hospital in September 1947 complaining of attacks of tightness and pain in the right upper part of the abdomen for the past 20 years. Prior to the onset of his symptoms he had had an attack of typhoid followed by dysentery in Ceylon in 1924. After recovery from that condition it was noted that he had acquired a slaty gray pigmentation, most pronounced on his face and arms.

Examination showed a well nourished man with decided pigmentation of the face and upper part of the body, less pronounced on the lower half of the trunk and on the legs. The temperature was normal. The liver was enlarged to the depth of 4 fingerbreadths below the costal margin, firm and painless and, except for a nodule in the epigastrium, smooth. No mucous membrane pigmentation was noticed. Investigations revealed the following: hemoglobin, 86 per cent (Haldane); red cell count, 4,480,000; color index, .96; serum protein, 6.0 Gm. per 100 ml.; fasting blood sugar, 0.90 Gm. per 100 cc.; glucose tolerance curve, within normal limits; stools, negative for parasites, ova and cysts, and urine, normal. A roentgenogram of the chest and stomach after a barium meal showed no abnormality. A piece of skin removed from the arm did not show any free iron but did show a distinct increase of melanin pigmentation in the basal layer. The patient was discharged with a diagnosis of hepatic cirrhosis associated with increased melanin pigmentation.

One year later the patient was readmitted with jaundice and gross loss of weight. He died shortly after admission and at autopsy was found to have cirrhosis of the liver and a primary carcinoma of the liver with secondary glandular metastases. The adrenal glands were normal.

CASE 3.—A woman aged 56 was admitted to hospital in May 1948 complaining of increased pigmentation which had been developing gradually over the past 11 years. More recently this had been associated with generalized pruritus, diarrhea and a loss of two stone (28 pounds [13 Kg.]) in weight.

Examination confirmed the loss of weight and increased darkening of the skin, most apparent on the flexures, nipples and vulva. The palms and soles were unaffected, and epidermal thickening was not noted. The buccal mucosa was free from pigmentation. The liver and spleen were both palpable 2 fingerbreadths below the costal margin. The urine was normal. Results on investigation were as follows: hemoglobin, 60 per cent; red blood cells, 3,200,000; white cells, 7,000, with a normal differential count; blood urea (after melena), 70 mg. per 100 ml.; blood sugar, 70 mg. per 100 ml.; blood sedimentation rate, 70 mm. in the first hour. The plasma bilirubin was 3.3 mg. and total plasma protein was 6.2 Gm. per 100 ml. with some increase in the globulin fraction.

Shortly after admission the patient had extensive melena, and on June 8 she had hematemesis and died in coma. Autopsy showed multilobular cirrhosis of the liver, splenic enlargement and esophageal varices. The adrenal glands appeared normal. A skin biopsy showed increased melanin pigmentation but did not show free iron.

CASE 4.—A woman aged 50 was admitted to the hospital in April 1949 complaining of darkening of the skin. She said that she had always been rather dark skinned but this pigmentation had become more pronounced recently. She had no other symptoms.

Examination showed a rather thin, dark-skinned woman, the pigmentation being most apparent on the flexures. The buccal mucosa was free from pigment. The respiratory systems and cardiovascular systems were essentially normal, and the blood pressure was 145/105. The liver was enlarged 4 fingerbreadths below the costal margin, and the spleen was easily palpable. Both organs were firm, smooth and painless. The urine was found to contain sugar, and the blood sugar curve was typically diabetic.

Investigations revealed the following: A skin biopsy showed increased melanin pigment but no free iron. A barium swallow and roentgenogram suggested a slight degree of varicosity at the lower end of the esophagus. Hemoglobin was 82 per cent; there was a normal white cell count, and plasma protein measured 6.5 Gm. (albumin, 4.6, and globulin, 1.9).

The patient was stabilized on insulin and was discharged. In August she was seen again, and it was noticed that her sclerotics were slightly jaundiced. The serum bilirubin was 4 mg. per 100 ml., and the plasma proteins were 5.75 Gm. The total 24-ketosteroid excretion in 24 hours was 3.1 mg., well within normal limits. A vaginal smear showed a normal postmenopausal epithelium. At the time of taking the smear it was noted that there was a small intracervical mucous polyp.

COMMENT

These four cases are considered to be examples of the same syndrome, liver cirrhosis associated with increased melanin pigmentation of the skin. From so small a number of cases it is not possible to draw conclusions about the prognosis, and probably it does not differ from that of other cases of progressive hepatic disease. The first three patients died, but the second person was pigmented for 20 years before seeking medical advice. Nevertheless, despite the subjective sense of well-being of the fourth patient, the early onset of jaundice makes the outlook unfavorable, and it is possible that the association of pigmentation betokens a severe degree of liver damage.

Before considering the possible mechanism of the pigment formation, I propose to discuss another pigmentary disease, acanthosis nigricans. There is some evidence indicating similarities between this condition and the cases described in this paper. Consideration of the pathology of one might help to explain the mechanism of the other.

ACANTHOSIS NIGRICANS

According to Curth (1948)[5] 420 cases of acanthosis nigricans, about 50 per cent of which have been associated with malignant disease, have been described. The condition is characterized by the development of pigmented, verrucous patches, most prominent in the axillas and groins, on the nipples, around the body orifices, on the palms of the hands, and—sometimes—on the mucous membranes. Less commonly the pigmentation and epithelial hypertrophy are generalized, affecting most of the cutaneous surface. As a rule the lesions are bilaterally symmetrical, but they may be unilateral in the "benign" type. The condition is classed as "benign" or "malignant" according to whether or not it is associated with cancer.

Curth (1936, 1943, 1948)[6] gives extensive reviews of all described cases and notes that of 208 cases of malignant acanthosis nigricans 93 per cent were associated with intra-abdominal carcinoma, the great majority with carcinoma of the stomach. A surprisingly large number of persons, considering the rarity of the disease, had primary carcinoma of the liver, although not all these diagnoses were confirmed histologically. Curth and Slanetz (1939)[7] also describe a dog with acanthosis nigricans and a primary cancer of the liver.

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6. Footnote 5. Curth, H. O.: Benign Type of Acanthosis Nigricans: Etiology, Arch. Dermat. & Syph. **34**:353 (Sept.) 1936; Cancer Associated with Acanthosis Nigricans: Review of Literature and Report of Case of Acanthosis Nigricans with Cancer of Breast, Arch. Surg. **47**:517 (Dec.) 1943.

7. Curth, H. O., and Slanetz, C. A.: Am. J. Cancer **37**:216, 1939.

Concerning the etiology of this condition there has been much discussion and but little agreement. It is fairly generally accepted that the skin condition itself is benign whether or not it is associated with cancer elsewhere. It would appear to be a nevoid lesion which is made manifest by some unknown mechanism.

By analogy with Addison's disease it has been thought that the pigmentation is due to involvement of the adrenal glands and the abdominal chromaffin tissue by secondary deposits of cancer. Full autopsies have not supported this theory, as in many cases the adrenal glands have been found free from metastases. Curth has suggested a genetic relationship between acanthosis nigricans and cancer. Certainly it would be difficult to explain the association of the two diseases without postulating some such basis for their coexistence, for, assuming for the moment that hepatic dysfunction is the cause of the appearance of the skin lesions, it would be necessary to explain why acanthosis nigricans does not appear with diseases of the liver other than primary carcinoma of that organ or possibly a hepatic disorder in association with cancer elsewhere. In any case, the "benign" type of acanthosis nigricans is a nevoid condition of the skin and, presumably, is a genetically inherited disorder. That the liver does play some part in the production of acanthosis nigricans I hope to demonstrate, but Curth's postulate of a genetic relationship between cancer and the skin disorder must be accepted although this does not give any precise information concerning the mechanism whereby the lesions are produced.

There remain uncertain theories of toxemia, avitaminosis and endocrine dysfunction, but none of these has been adequately examined. Curth considers that the steroid hormones might have something to do with the disease but does not elaborate the suggestion. It is the object of this paper to consider this hypothesis more fully, but before that is done it will be necessary to discuss some recent investigations into the mechanism of melanin formation in the skin.

MELANIN PIGMENTATION

It is not proposed to consider in detail the chemical mechanism of melanin formation. In brief, there is evidence for the presence in the skin of a specific oxidase or series of oxidases (Ginsberg, 1944; Greenstein and associates, 1944)[8] which act on tyrosine or dihydroxyphenylalanine to form melanin. It is probable that these oxidases are held in check by certain reducing substances, notably sulfhydryls and ascorbic acid. Before the oxidases can function it is necessary that a stimulus should be applied which will inactivate these reducing chemicals. There is evidence that many varying stimuli can perform this office.

Figge (1940)[9] has demonstrated the inhibiting action of glutathione, preventing the in vitro oxidation of *l*-tyrosine by tyrosinase, and Figge and Allen (1941)[10] have further shown that this inhibition can be overcome by the addition of estrone to the substrate. This observation has been criticized recently by Lerner and Fitzpatrick (1950)[11] on the grounds that the tyrosinase used was a crude preparation

8. Ginsberg, B.: Genetics **29**:176, 1944. Greenstein, J. P.; Werne, J.; Eschenbrenner, A. B., and Leuthardt, F. H.: J. Nat. Cancer Inst. **5**:55, 1944.

9. Figge, F. H. J.: J. Cell. & Comp. Physiol. **15**:233, 1940.

10. Figge, F. H. J., and Allen, E.: Endocrinology **29**:262, 1941.

11. Lerner, A. B., and Fitzpatrick, T. B.: Physiol. Rev. **30**:91, 1950.

probably containing estrinase. So it is open to doubt whether the inhibition was due to the estrone or to some metabolic product of the hormone or whether the estrone was itself oxidized to some colored product.

Rothman and his colleagues (1946)[12] have described the presence of a sulfhydryl substance in the skin which inhibits the oxidation of tyrosine and "dopa" by tyrosinase. Flesch (1949)[13] notes that the extractable sulfhydryl content of the skin is diminished by ultraviolet irradiation, and it is considered that this action is due to the conversion of the sulfhydryl from the reduced to the oxidized form. Woodward (1933)[14] has shown that glutathione is oxidized when exposed to ultraviolet radiation. Flesch, comparing aqueous extracts of the epidermis with solutions of cysteine and glutathione, found that the epidermal extract was 2.5 times more potent than the glutathione and the glutathione 13 times more effective than cysteine in inhibiting tyrosinase. It is possible that the epidermal extract contained small quantities of ascorbic acid, which, as shown by Hopkins and Morgan (1936),[15] protects glutathione from oxidation while it is itself oxidized to dehydroascorbic acid.

The evidence suggests, therefore, that the inhibiting agent of tyrosinase in the skin is glutathione, possibly acting in conjunction with ascorbic acid. It is possible that circulating estrogen is one of the agents whereby these inhibiting substances are themselves neutralized. This possibility is still unproved and can be considered only an attractive hypothesis. Nevertheless, the clinical evidence certainly suggests that estrogen can lead to melanin pigmentation under certain circumstances.

THE LIVER AND ESTROGEN METABOLISM

It is fairly well established that circulating estrogens are detoxicated by the liver either by conversion to ethereal sulfates or by conjunction with glucuronic acid. More recent work by Cantarow and his colleagues (1943)[16] suggests that some estrogen is removed from circulation by excretion in the bile. The whole problem is reviewed by Jailer (1949).[17]

Talbot (1939)[18] showed that rats poisoned with carbon tetrachloride failed to detoxicate estrogens, the degree of impairment in this function being correlated with the degree of liver damage. Pincus and Martin (1940)[19] confirmed this experiment, and Heller (1940)[20] found that liver slices were able to destroy or neutralize estrogen. Greenstein (1947)[21] remarks that there is a depression of hepatic activity

12. Rothman, S.; Krysa, H. F., and Smiljanic, A. M.: Proc. Soc. Exper. Biol. & Med. **62**:208, 1946.

13. Flesch, P.: Proc. Soc. Exper. Biol. & Med. **70**:136, 1949.

14. Woodward, G. E.: Biochem. J. **27**:1411, 1933.

15. Hopkins, F. G., and Morgan, E. J.: Biochem. J. **30**:1446, 1936.

16. Cantarow, A.; Paschkis, K. E.; Rakoff, A. E., and Hansen, L. P.: Endocrinology **33**:309, 1943.

17. Jailer, J. W.: J. Clin. Endocrinol. **9**:557, 1949.

18. Talbot, N. B.: Endocrinology **25**:601, 1939.

19. Pincus, G., and Martin, D. W.: Endocrinology **27**:838, 1940.

20. Heller, C. G.: Endocrinology **26**:619, 1940.

21. Greenstein, J. P.: Biochemistry of Cancer, New York, Academic Press, Inc., 1947.

in malignant disease, and Zondek and Black (1947)[22] describe an estrogen clearance test by which they demonstrated impairment of estrogen inactivation in severe cases of infective hepatitis.

There is a considerable amount of evidence to suggest that the vitamin B complex has something to do with this detoxicating mechanism. Biskind and Biskind (1941),[23] using the technique of splenic implants of estrogens in rats, showed that deprivation of the vitamin B complex led to a failure in the inactivation of estrogen. This work was further amplified by Biskind and Shelesnyak (1942),[24] who confirmed the first result. Segaloff and Segaloff (1944)[25] found that the hepatic insufficiency could be corrected by the administration of thiamine and riboflavin but not when other members of the B group of vitamins were administered. The whole subject is extensively reviewed by Biskind and Biskind (1946).[26]

Germane to this theory are the observations of Jacobs [2] and of Klatskin and his colleagues (1947),[27] who describe gynecomastia in soldiers returning from Japanese prisoner of war camps. It is suggested that deprivation of food and the necessary vitamins led to an impairment of liver function. When an ample diet was given the estrogen level rose before the liver had fully recovered, this occurrence leading to a transient breast enlargement.

THE MECHANISM OF PIGMENTATION IN HEPATIC CIRRHOSIS AND ACANTHOSIS NIGRICANS

To explain the phenomenon of pigmentation in hepatic disease and in acanthosis nigricans the following hypothesis is proposed: In cases of severe liver damage or relative insufficiency there is a failure of the estrogen-detoxicating mechanism. The free circulating estrogen possibly acts on the skin sulfhydryls and so releases the melanin-forming oxidases.

The liver is in a damaged state when cirrhotic or when invaded by carcinoma. At puberty, when the lesions of "benign" acanthosis nigricans usually make their appearance, the estrogen content of the blood is increased and the liver fails to detoxicate it adequately. Some such mechanism is likely to be responsible for the gynecomastia of puberty. In hepatic cirrhosis, in carcinoma—and particularly carcinoma of the stomach—the degree of cachexia is pronounced, so that it is reasonable to suggest that food and vitamin absorption are impaired, this fact leading to further interference with estrogen metabolism by a liver already damaged. The comparatively large number of cases of primary carcinoma of the liver in Curth's series of cases of acanthosis nigricans suggests that the liver is in some way involved in the production of the skin pigmentation. In the second case described in this paper the patient died from cirrhosis and primary carcinoma of the liver. A number of cases of acanthosis nigricans associated with intrathoracic carcinoma have been described, and Ellenbogen (1949) [28] gives an account of two cases of carcinoma of the lung in which the pigmentation was generalized. The degree of cachexia in

22. Zondek, B., and Black, R.: J. Clin. Endocrinol. **7**:519, 1947.
23. Biskind, M. S., and Biskind, G. R.: Science **94**:462, 1941.
24. Biskind, M. S., and Shelesnyak, M. C.: Endocrinology **30**:819, 1942.
25. Segaloff, A., and Segaloff, A.: Endocrinology **34**:346, 1944.
26. Biskind, G. R., and Biskind, M. S.: Am. J. Clin. Path. **16**:737, 1946.
27. Klatskin, G.; Salter, W. T., and Humm, F. D.: Am. J. M. Sc. **213**:19, 1947.
28. Ellenbogen, B. K.: Brit. J. Dermat. **61**:251, 1949.

each case was appreciable, and in one case there were secondary deposits in the liver. Of considerable interest is the case of acanthosis nigricans described by Hollander (1943).[29] The patient had a gastric carcinoma, and the skin lesions are said to have regressed after injections of vitamin B complex. It seems improbable that the vitamin was directly responsible for the improvement in the skin lesions, but it may have had some effect on the estrogen-detoxicating function of the liver.

If this hypothesis is to be substantiated a number of objections have to be met. Carcinoma and hepatic cirrhosis are common, whereas associated pigmentation and acanthosis nigricans are rare. In order to explain this discrepancy one must presuppose a specific skin sensitivity in some patients. If it is accepted that estrogens are responsible for the appearance of spider nevi, pigmented moles and palmar erythema in pregnancy, one must assume a specific sensitivity to estrogen of certain skin structures, for by no means all pregnant women exhibit all or any of these skin changes. It is agreed that between acanthosis nigricans—a nevoid condition of the skin—and carcinoma there exists a genetic relationship. The estrogen stimulus at puberty, or when the liver is damaged, is merely the means whereby the skin nevus is made manifest. It is not easy to say whether skin pigmentation associated with hepatic cirrhosis is rare. The four cases described in this paper were seen by pure chance, and it is probable—as I gather from discussion of the cases with colleagues—that the skin change is usually overshadowed by the more important hepatic disease. Nevertheless, not all cases of cirrhosis show pigmentation, and neither do all cases of cirrhosis show gynecomastia or vascular nevi. Either the degree of impairment of estrogen metabolism varies, or, more probably, there is a specific tissue sensitivity to estrogen which in one case produces palmar erythema and in another generalized pigmentation.

Of the four patients with cirrhosis described three were postmenopausal women and the other was a man. Most cases of "malignant" acanthosis nigricans are in persons beyond middle age, and it might be objected that in all these cases the quantity of circulating estrogen would be small. The first three patients in the series reported here died before any estrogen studies were possible, and, although it has not been possible to make a bioassay of urinary estrogen in the fourth case, the vaginal epithelium was reported as being typically postmenopausal. If, however, it is accepted that the gynecomastia of starvation is due to circulating active estrogen, then the same objection applies in cases of that sort, although in the cases of gynecomastia and cirrhosis described by Glass and his associates (1940) [8] a high "free" urinary estrogen was found. Once again it seems that a specific tissue sensitivity to estrogen is responsible for the change, and in the fourth case a quantity of estrogen which is insufficient to change a postmenopausal epithelium to a premenopausal one might be adequate to produce pigmentation of a skin so predisposed.

A more serious objection is raised by Zondek and Brzezinski (1948),[30] who examined the estrogen metabolism of women with severe degrees of malnutrition and vitamin deficiency with clinical symptoms of ariboflavinosis and pellagra. The patients were pregnant women, nonpregnant women of child-bearing age and pregnant women with infective hepatitis. No signs of failure to detoxicate estro-

29. Hollander, L.: Acanthosis Nigricans: Is It a Form of Avitaminosis? Arch. Dermat. & Syph. **48**:650 (Dec.) 1943.

30. Zondek, B., and Brzezinski: J. Obst. & Gynaec. Brit. Emp. **55**:273, 1948.

gens, whether endogenous or injected, were discovered. Hooker and his colleagues (1947) [31] likewise found that castrated female monkeys treated with splenic implants of estrogens exhibited typical endometrial and vaginal changes from estrogen stimulation. In short, whereas it might be accepted that the livers of rats and of other lower mammals detoxicate estrogens, the evidence for a similar mechanism in man and other primates is, to say the least, inconclusive.

It should be noted, however, that all the patients in Zondek's paper were of child-bearing age while the female patients described in this paper were postmenopausal. The patients with gynecomastia associated with hepatic cirrhosis whose cases were described by Glass and his associates (1944) [32] were, for obvious reasons, male, but the patients with infective hepatitis whose cases were described by Gilder and Hoagland (1946)[33] were also all male. These workers found an increased urinary content of active estrogen which persisted well into the period of convalesence and correlated the quantity of estrogen with the degree of liver damage. Pregnant women sometimes manifest palmar erythema and vascular nevi, changes thought to be due to estrogen action. But not all pregnant women show any of these changes, and, leaving aside the question of tissue sensitivity, the quantity of estrogen circulating makes these cases not comparable with those of the male and the postmenopausal women described. It would be interesting to know what part is played by the pituitary hormones in the production of these conflicting results.

The conflict of evidence described in this paper shows that the problem of estrogen inactivation in man is by no means settled. It seems probable that the mechanism in the woman of child-bearing age differs from that in men and postmenopausal women. Alternatively, between the menarche and the menopause the liver is more capable of dealing with large quantities of estrogen or the tissues are less sensitive to its effects. The theory outlined concerning the role of estrogen in the production of melanin pigmentation is founded on the experimental and clinical evidence of estrogen inactivation by the liver. The evidence is by no means conclusive, and much experimental work remains to be done on the subject. It is hoped that this paper will stimulate further interest in the problems that have been raised.

SUMMARY

Four cases of generalized melanin pigmentation of the skin associated with hepatic cirrhosis are described.

The etiology of acanthosis nigricans, the biochemical mechanism of melanin formation and the part played by the liver in the inactivation of estrogen are all briefly discussed.

A theory is proposed attempting to explain the pigmentation in the four cases of hepatic cirrhosis and the development of the pigmented lesions of acanthosis nigricans.

Sir Lionel Whitby gave me permission to use the first two case reports, previously employed in my Cambridge M.D. thesis; Dr. C. R. Croft and Dr. R. H. Blair allowed me to examine their cases, and Dr. P. E. Hughesdon examined and reported on the vaginal smear taken in case 4.

31. Hooker, C. W.; Drill, V. A., and Pfeiffer, C. A.: Proc. Soc. Exper. Biol. & Med. **65**:192, 1947.

32. Glass, S. J.; Edmondson, H. A., and Soll, S. N.: J. Clin. Endocrinol. **4**:54, 1944.

33. Gilder, H., and Hoagland, C. L.: Proc. Soc. Exper. Biol. & Med. **61**:62, 1946.

FURTHER STUDIES IN AUTOECZEMATIZATION

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IN A PREVIOUS report,[1] preliminary studies concerning the nature of autoeczematization were described. Patients with autoeczematization secondary to various types of eczematous dermatoses were tested intradermally with autogenous extracts of scale, leukocytes and blood plasma. Positive reactions to scale extracts were obtained in a significant proportion of cases. The results of skin testing with the various substances indicated that autoeczematization is a true allergic reaction and that the antigen responsible for the distal eczematous process is apparently a water-soluble fraction of epidermal cells. The development of doubtful reactions to leukocytes in a few instances raised the question as to their possible role in the transportation of the epidermal antigen from the primary eczematous focus.

As a result of this preliminary study it was felt that the specificity of the scale antigen should be confirmed, its mode of transportation determined aad the importance of the eosinophil in this process evaluated. These aspects of the problem are the subject of the present investigation.

NOTE ON METHODS

The method of preparation of the various test substances was identical with that described in the previous report. The final method of scale antigen preparation, utilizing an undiluted saline extract of ether-washed scales, was employed in all cases.

The number of eosinophils present per cubic millimeter of blood was determined on each patient, according to the method of Thorn and his associates,[2] and persons with eosinophilia were selected for special testing. The special tests for this selected group included intradermal testing with autogenous leukocyte suspensions and the determination of blood eosinophil response four hours after the subcutaneous injection of 0.5 cc. of a 1:1,000 solution of epinephrine. In addition, these patients were observed closely for a 48 hour period after the injection for any evidence of clinical progression.

Twenty patients with autoeczematization were studied in the present series; all patients were tested with scale extract, and data on an additional four patients tested similarly in the previous study were included in the analysis of the results. Six patients with eosinophilia received the special tests listed above. Fourteen of the patients were tested with autogenous

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1. Cormia, F. E., and Esplin, B. M.: Autoeczematization: Preliminary Report, Arch. Dermat. & Syph. **61**:931 (June) 1950.

2. Thorn, G. W.; Forsham, P. H.; Prunty, F. T. G., and Hills, A. G.: A Test for Adrenal Cortical Insufficiency: Response to Adrenocorticotropic Hormone, J. A. M. A. **137**:1005 (July 17) 1948; correction, ibid. **137**:1544 (Aug. 21) 1948.

cantharides blister fluid, and the results were considered together with those obtained for four patients previously tested. Control experiments with scale extract were performed on 26 patients, and with blister fluid on 11 patients. No additional leukocyte controls were done.

RESULTS OF EXPERIMENTS

The results of testing with autogenous scale extracts are summarized in table 1.

Of the 24 patients tested, positive immediate reactions were obtained in 50 per cent, positive delayed reactions in 54 per cent and doubtful delayed reactions in 16 per cent. Further analysis of the data revealed that 79 per cent of the patients had some type of reaction, either immediate or delayed. The superiority of this scale extract over that originally used is attested by the fact that in the earlier series

TABLE 1.—*Results of Tests with Autogenous Scale Extracts*

Primary Reaction Type	No. of Subjects	Reactions to Scale Extract	
		Immediate	Delayed
Contact	11	5	6 (2±)
Stasis	4	3	2 (1±)
Seborrheic	3	0	3
Nummular	2	2	1
Dermatophytosis	2	1	0 (1±)
Atopic	1	0	0
Infectious eczema	1	1	1
Total	24	12	13 (4±)
Controls	26	2	1

TABLE 2.—*Experiments Utilizing Autogeneous Leukocyte and Scale Extracts from Patients with Eosinophilia*

Primary Reaction Type	Eosinophil Count/Cubic Millimeter		Clinical Exacerbation After Epinephrine	Reactions to Intradermal Tests			
				Autogenous Leukocyte Extract		Autogenous Scale Extract	
	Initial	After Epinephrine*		Immediate	Delayed	Immediate	Delayed
Contact	630	310	+	0	0	0	+
	545	186	0	0	±	0	+
	390	ND †	—	0	+	0	0
Stasis	391	223	0	0	+	0	0
Nummular	1,420	1,256	+	+	0	+	+
Dermatophytosis	540	335	+	+	+	+	±

* Four hours after administration of epinephrine (1:1,000), 0.5 cc. subcutaneously.
† No decrease.

only 41 per cent of the patients had positive immediate reactions and but 29 per cent had delayed responses.

Positive immediate reactions were obtained in 8 per cent and positive delayed reactions in 3 per cent of the 26 control patients. The infrequency of reactions in the control series tends to confirm the significance of positive reactions to autogenous scale extracts in patients with autoeczematization.

A second experiment was conducted in an effort to clarify the role of leukocytes in the transportation of antigen. Since Godlowski,[3] on the basis of animal experiments, has reported that antigen is transported only by eosinophilic leuko-

3. Godlowski, Z. Z.: Transportation of the Anaphylactogenic Property by Eosinophil, Brit. J. Exper. Path. **29**:511 (Dec.) 1948.

cytes, it seemed worth while to make additional studies in autoeczematous patients with eosinophilia. The results of these studies are summarized in table 2.

In this group of six patients an eosinophil count ranging from 390 to 1,420 per cubic millimeter was present. After the administration of epinephrine a significant decrease in eosinophils was demonstrated in five patients tested. In three of these five patients a definite exacerbation of the autoeczematous process supervened within a 12 hour period after epinephrine was given.

Positive immediate reactions to autogenous leukocyte suspensions were obtained in two, positive delayed reactions in three and a doubtful delayed reaction in one of six patients tested. These observations may be contrasted with an absence of delayed reactions to leukocyte suspension in nine previously tested control subjects. The reactions of this group of patients to scale extract have been recorded in table 2 for comparison with results obtained from reactions to leukocyte suspension. As will be noted, a positive correlation exists in half the cases.

The results of intradermal testing with autogenous cantharides blister fluid are summarized in table 3.

Fluid obtained from a blister produced by cantharides plaster was found to be a primary irritant, as shown by the frequency of positive immediate reactions in con-

TABLE 3.—*Results of Intradermal Tests with Autogenous Cantharides Blister Fluid*

	No. Tested	No. of Reactions	
		Immediate	Delayed
Patients	18	10 (1±)	1 *
Controls	11	10	2 *

* Persistence of immediate reaction for 48 hours.

trol subjects. In 3 per cent of the subjects tested immediate reactions were of sufficient severity to persist throughout a 48 hour period.

COMMENTS

The results herein reported tend to confirm the previous impression that a water-soluble fraction of epidermal cells is the antigen responsible for the production of autoeczematization. It is evident that the antigen as presently extracted is still in a crude form since positive reactions are not uniformly obtained. The lack of complete correlation between reactions to scale extract and those to leukocyte suspension in given patients, as shown in table 2, is further evidence of the comparatively low potency of the extracted antigens.

Presumably other factors, such as bacterial infections or specific contact sensitizations, may potentiate the autoeczematous response. However, in the latter situation, patients with contact sensitizations, verified by patch testing, had as high an incidence of positive reactions to epidermal antigen as did those with other types of antecedent dermatitis.

In the evaluation of the reactions to scale extracts, it is noteworthy that each patient was tested with an antigen prepared from his own scales. The results obtained, therefore, would seemingly be of greater significance than those reported by other investigators who used homologous rather than autogenous scale extract

as sources of antigen. Be that as it may, Simon [4] has pointed out that a common antigen may be present in all human dander. In this connection, a patient of this series who acquired autoeczematization after a contact dermatitis is of interest. A positive delayed reaction was obtained to autogenous scale extract. Subsequent relapses were traced to contact with her husband's dander, an extract of which produced a strongly positive reaction in the patient.

An attempt was made to extract in purer form the water-soluble antigen from the epidermis by means of a bulla produced by cantharides plaster. This maneuver was unsuccessful, since the blister fluid not only produced false positive immediate reactions in controls but also failed to produce any positive delayed reactions in patients with autoeczematization.

The experiments recorded in table 2 were performed in an effort to evaluate the role of the eosinophils in the transportation of epidermal antigen. If this antigen is transported by eosinophils, intradermal tests with a leukocyte suspension containing a relatively high proportion of them should produce positive delayed reactions. It is of interest that one doubtful and three positive delayed reactions were obtained in six patients tested. This result may be contrasted with that obtained in the previous series, in which only three doubtful reactions were elicited in 30 patients tested. In the previous group no attempt at selection on a basis of eosinophilia was made.

Reference should be made again to the only partial correlation between positive reactions to leukocyte suspensions and those to scale extracts. Moreover, the failure to obtain positive reactions with leukocyte suspensions in all cases tested may be due to an insufficient concentration of eosinophils in the suspension. This difficulty might be obviated by the use of larger amounts of blood, perhaps up to 50 cc., for the extraction of leukocytes.

The role of the eosinophils in antigen transfer was further investigated after the subcutaneous use of epinephrine. If this procedure results in the destruction of eosinophils through adrenal cortical stimulation, the liberation of antigen in increased amounts should result in a clinical exacerbation of the autoeczematous process. Such exacerbation was noted in three out of five patients tested. In another patient not included in the present series, a severe contact dermatitis involving the face was complicated by extensive autoeczematization within three hours after the injection of 1 cc. of a 1 : 1,000 solution of epinephrine.

The development of distal eczematization has been observed also in many patients with acute dermatitis treated by X radiation. In these patients a similar mechanism may be operating, since a characteristic effect of X rays is the local destruction of leukocytes. Furthermore, the rapid destruction of leukocytes may liberate proteolytic enzymes which in turn facilitate the absorption of epidermal antigen.

It is possible too that clinical progression seen not infrequently after the use of autohemotherapy may be due to the liberation of antigens from destroyed leukocytes. Another interesting phenomenon has been the development of dermatitis in traumatized areas in patients with autoeczematization. This was produced deliberately in some of the patients studied by the rubbing of an uninvolved area of skin

4. Simon, F. A.: The Allergen of Human Dander Present in Skin of the General Body Surface, J. Invest. Dermat. **9**:329 (Dec.) 1947.

for 10 minutes three times a day for two days. The influence of trauma after solar radiation was shown dramatically in one other patient who had a beginning autoeczematization of the legs complicating a contact dermatitis of the feet. As a therapeutic measure, the patient exposed herself to the sun for a considerable period. As a result, all areas not covered by her bathing suit became the site of a severe autoeczematous reaction.

A survey of the results documented in the above experiments suggests, as did the preliminary experimental work, that the antigen responsible for autoeczematization may be derived from epidermal cells. If this is true the epidermal allergen may act as a complete antigen or possibly may be combined with bacterial products or other substances to form a combined antigen. More investigation is desirable to clarify this point. The above experiments suggest also, but by no means prove, that the epidermal antigen may be transported from its source by eosinophilic leukocytes. This question also requires further clarification. In addition, fundamental studies on antibody formation and transportation are urgently needed. Utilization of leukocytes for passive transfer tests, as recently studied by Lawrence,[5] might be of value in the elucidation of this phase of the problem. Surely the employment of modern investigative techniques in cooperative studies may further clarify the pathogenesis of the autoeczematous reaction.

SUMMARY

Further studies have been made concerning the nature of autoeczematization.

In confirmation of previous studies, it is believed that the antigen involved is a water-soluble component of epidermal cells.

Additional experiments suggest that the antigen may be transported from the primary eczematous site by eosinophilic leukocytes, but the evidence that this actually happens is by no means conclusive.

Some factors influencing the development of autoeczematization have been discussed.

5. Lawrence, H. S.: Cellular Transfer of Cutaneous Hypersensitivity to Tuberculin in Man, Proc. Soc. Exper. Biol. & Med. **71**:516 (Aug.) 1949.

ERYTHRODERMA ICHTHYOSIFORME CONGENITUM

Epidermotectoscopical Description of a Case

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SUŠAK, JUGOSLAVIA

BROCQ, IN 1902, was the first to describe the congenital disease characterized by erythroderma and hyperkeratosis of an ichthyosiform character covering the whole body. Later on, besides Brocq, many other authors (Thibierge, Riecke and Jadassohn) stated in their works that they considered this disease, which differs in many details from ichthyosis, a particular pathological entity. Other writers, however (Bruhns, Meneau and Ingermann), referring to intermediary cases which did not show the characteristics stated, expressed contrary views.

CLINICAL FEATURES

Erythroderma ichthyosiforme congenitum appears usually immediately after birth and much more seldom in early childhood. Its main morphological features are distinct and generalized hyperkeratosis and erythroderma.

Both symptoms vary in their intensity and extent in individual cases and usually assume a progressive course. Hyperkeratotic changes in the form of thick, dry and polygonal scales are most remarkable in the axillas, cubital and popliteal fossae and the folds of the joints. In some cases erythematous changes cover the whole skin, but most usually the red color is visible in the face, where hyperkeratosis is insignificant, and also under the scales on the skin of the body. Palms and soles are covered with thick horny layers, and the nails are thickened and deformed. The growth of hair and nails is speeded up. The scalp is covered with seborrheic scales. The skin of the face is tight, shiny and red, with an ectropion. Hyperhidrosis is intensified in the face, axillas, palms and soles. Bullous formations are more seldom met in erythroderma ichthyosiforme congenitum. Some authors think these formations arise spontaneously; others consider them of traumatic or impetiginous origin.

Following is a report of a case of erythroderma ichthyosiforme congenitum. In it is described a method I elaborated, called epidermotectoscopy, since it may perhaps prove efficacious in differential diagnosis.

REPORT OF CASE

B. T., a boy aged 14, whose parents and two brothers showed no signs of a similar disease, was a healthy and well developed young man of normal intelligence and in a good state of nutrition. His parents had noticed immediately after his birth that his skin was of a bright red color, and a short time later it had begun to scale off. While the red color gradually lost its brightness the scaly layers, however, became more and more distinct, and after some years

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the body assumed its appearance at the time of writing; i. e., the trunk and the limbs became almost entirely covered with scales, and the face and the auricles were red. Also, later, the thickening of the skin of the hands and soles advanced gradually. The patient had been experiencing during the last years considerable difficulty when bending his fingers or closing his fists. Three years ago he had had nephritis. There was considerable sweating of the face, palms and soles and in the axillas. Heat and cold were endured well. The boy did not notice any influence of any factor on the state of skin. He never had had any bullous changes on the skin. He had always been treated with ointments only.

Clinical Findings.—The hair was normal in density and dry. The scalp was covered with thick and dry seborrheic scales. The teeth were normal. No changes were visible on the mucous membranes. The skin of the face and the auricles was a little tightened, red and shiny. On the cheeks, nose and auricles telangiectasias were distinctly visible. The upper eyelids and the parts around the mouth were delicately wrinkled and covered with fine scales. When the eyes were closed the lids remained about 2 mm. apart. There was no ectropion. The whole neck, trunk and limbs were covered with scales. They were quadrangular or polygonal and similar to those of ichthyosis. They were particularly thick and dark on the neck, axillas, cubital and popliteal spaces and the knees and elbows. In some places they stuck fast to the skin, and in others they could be easily lifted off. Palms and soles were covered with thick hyperkeratotic layers which were particularly thick and coarse along the edges. The skin of the fingers was

Fig. 1.—Clinical appearance of the patient in the reported case.

tightened and sclerotic, and the fingers themselves were thinned. The patient could neither open nor close his fist perfectly, and his hands appeared as in sclerodactylia (fig. 1).

The x-ray examination revealed that the bones of the hands, especially of the wrist, bases of the metacarpals and finger phalanges, were rarefied and decalcified. They showed a coarse and rebuilt structure. The spaces between the joints of the wrist and the metacarpus were widened. The interdigital folds went higher than usual.

Examination of the internal organs revealed nothing abnormal. Results in all laboratory studies were normal. The Kahn and Wassermann reactions were negative.

Histological Observations.—The histological examination of a piece of skin cut out from the extensor area of the upper arm revealed the following changes: The stratum corneum was considerably thickened and showed a lamellary structure. In some places the structure was netlike. No nucleus was observed in the cells. The stratum corneum joined the stratum granulosum in a wavelike line, and the stratum granulosum was preserved in its continuity. In some places it grew thicker by 5 to 6 layers, and it was thinner in others. The stratum malpighii was thickened, especially in the interpapillary spaces. The basal membrane was everywhere well preserved, particularly in the sites of confluent papillae, where it was sharply marked. In the deeper hypodermal tissue there was a large number of swollen gland orifices; their cells had large round nuclei which could be readily stained. Some sweat and oil glands and follicles did not show any changes. In the upper layers of the hypodermal tissue there were small nests and scattered lines of inflammatory infiltrations consisting mainly of mononuclear and polynuclear cells (fig. 2).

INVESTIGATIONS BY MEANS OF EPIDERMOTECTOSCOPY [1]

The method of investigation known as epidermotectoscopy, elaborated by me and my associates, is carried out as follows: After careful cleansing of the skin with alcohol, any possible rubbing having been avoided, a thin layer from the some-

Fig. 2.—Histological features in the reported case.

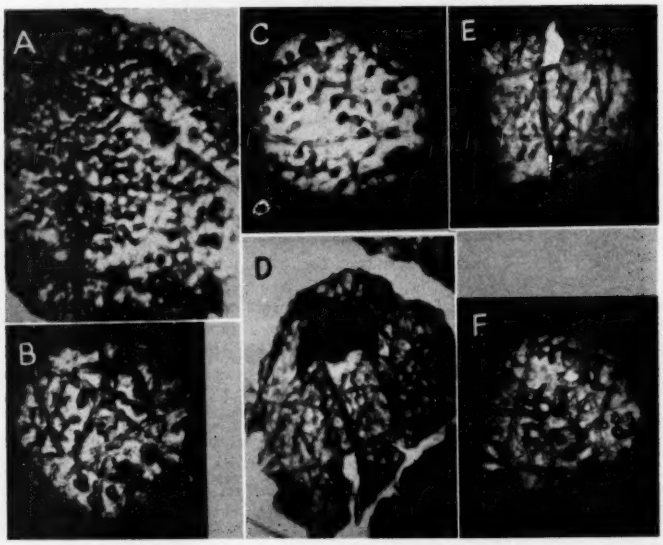

Fig. 3.—*A* (× 15), *B* (× 30) and *C* (× 30) show the epidermotectoscopical view in the reported case of erythroderma ichthyosiforme congenitum. *D* (× 15), *E* (× 30) and *F* (× 30) illustrate the epidermal morphologic features in ichthyosis vulgaris.

what tight efflorescence parallel to the skin surface is cut off with a fine, sharp knife, put on a slide and directly examined under a microscope with a 30 fold or,

1. Vukas, A.: Application of Tangential Cuts of Skin Efflorescences as a Method Important in Differential Diagnosis and in the Examination of Skin Diseases (Epidermotectoscopy), Acta med. jugoslavica **4**:1-2, 1950.

if necessary, 50 fold magnification. The specimen is removed from sensitive patients with the use of a local anesthetic (subcutaneous squirting of the efflorescence with 2 per cent procaine hydrochloride solution), and from less sensitive ones without anesthetic.

This method permits one to study precisely the surface architectonics of the epidermis, since with it there are to be detected epidermal pathological alterations in an up to now unusual perspective.[2]

Parts *A* ($\times$ 15), *B* ($\times$ 30) and *C* ($\times$ 30) of figure 3 show the epidermotectoscopical view in our case of erythroderma ichthyosiforme. These epidermotectograms taken from various regions show perfectly the epidermal pathological configuration of the skin in our case.

Parts *D* ($\times$ 15), *E* ($\times$ 30) and *F* ($\times$ 30) of figure 3 illustrate the epidermal morphologic features of the skin in ichthyosis vulgaris.

Although certain differences can be noticed in the epidermal pathological configuration by comparison of epidermotectograms of these diseases, it is not possible for me to make a detailed analysis of this superficial morphologic picture for the purpose of differential diagnosis on the basis of only one case of erythroderma ichthyosiforme congenitum.

Unfortunately we had so far no opportunity to examine epidermotectoscopically other forms of generalized and localized ichthyosis as well as naevus verrucosus, considered to be the same pathological entity.

COMMENT

In our case the symptomatology corresponded perfectly to Brocq's description of this disease. The disorder set in immediately after birth and assumed a progressive course. At the beginning erythroderma covered the whole skin, but later it became restricted to the face. The generalized hyperkeratosis of an ichthyosiform aspect showed predominantly inverse localization in comparison with that of ichthyosis. Hyperkeratosis of palms and soles, with alterations of nails, and considerable seborrhea capitis were also present. The histopathological picture was characteristic.

In differential diagnosis in this case, with its rich and characteristic symptomatology, only ichthyosis, a disease still considered by many authors to be identical with erythroderma ichthyosiforme congenitum, should be considered.

The strict congenitality, inverse localization of hyperkeratotic changes with alterations of palms, soles and nails and the distinct erythroderma all do not correspond to the clinical symptomatology of ichthyosis vulgaris. Ichthyosis vulgaris shows, if histologically examined, a thickened stratum corneum, a thinned or completely missing stratum granulosum, a thinned stratum spinosum, well developed papillae and involvement of sudoriferous and sebaceous glands. The histopathological observations in our case differed considerably from those in ichthyosis vulgaris.

As for ichthyosis congenita (Ricke, Siemens) the clinical and histological morphologic features are identical with those of erythroderma ichthyosiforme congenitum, and these conditions are therefore considered to be the same pathological entity.

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2. Vukas, A.: Zur Kenntnis der Epidermodysplasia verruciformis, Dermatologica **101**:37-41, 1950.

Though the comparison of the epidermotectograms of erythroderma ichthyosiforme congenitum with those of ichthyosis vulgaris does show certain differences in the configuration of the pathological epidermis, no conclusions whatsoever may be drawn on the basis of a single case. But this method applied to a large enough series seems to offer certain prospects because of the analysis of the details, which might demonstrate sharper and better defined differences. Accordingly I believe I am justified in recommending the application of this method on a larger scale.

Keeping in mind that superficial architecture is the expression of pathophysiological occurrences in the epidermis in all their phases, it would be a mistake to expect lasting and unchanged epidermotectoscopical forms, but in the individual phases of development of various conditions these forms have still their particular characteristics and consequently also their diagnostic importance.

SUMMARY

A typical case of erythroderma ichthyosiforme congenitum with distinct clinical features which perfectly correspond to Brocq's description of that disease is presented. The histopathological picture corresponds also to that described for this rare kind of dermatosis.

Besides the clinical and histopathological report, a demonstration of the superficial architectonics of a case by means of the author's own method, named epidermotectoscopy, is given.

The superficial morphologic features of the reported case are compared with those of ichthyosis vulgaris, which is the most important condition in differential diagnosis in cases of erythroderma ichthyosiforme congenitum. Further investigations in that direction, because only one case of that disease was at the author's disposal, are indicated.

TREATMENT OF SEBORRHEIC DERMATITIS WITH A SHAMPOO CONTAINING SELENIUM DISULFIDE

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SULFUR has long been used in general therapeusis. From the very inception of dermatological literature, sulfur compounds and preparations have been recommended for the therapy of a great variety of dermatoses, particularly parasitic infestations and seborrheic dermatitis.

In the search for newer and more efficient substances in the topical treatment of the seborrheic dermatoses, selenium was considered for therapeutic trial because of its general properties and the group relationship of sulfur and selenium which was described by the periodic law of Mendelejeff. It seemed not unreasonable to suspect that similar and possibly more effective therapeutic properties would be exhibited if selenium were used in the conditions for which sulfur has proved to be of some value.

The immediate clinical application of a preparation containing a selenium compound was regarded with considerable reservation in view of the many toxicological effects of selenium abundantly described in the literature since 1842.[1] On the other hand, although it is known that a number of organic and inorganic selenium compounds penetrate the intact skin,[2] few observations have been carried out on

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Selenium-containing shampoo was supplied by the Battelle Memorial Institute, Columbus, Ohio.

From the Department of Dermatology and Syphilology, Leon Goldman, M.D., director, and the Kettering Laboratory in the Department of Preventive Medicine and Industrial Health, College of Medicine, Robert A. Kehoe, M.D., director, University of Cincinnati.

1. Japha, A.: Experimenta nonnulla de vi selenii in organismum animalem, Halis, formis Ploetzianis, 1842. Madison, T. C.: Sanitary Report: Fort Randall, in Coolidge, R. H.: Statistical Report on the Sickness and Mortality in the Army of the U. S., Jan. 1855-Jan. 1860, Compiled from the records of the Surgeon General's and Adjutant General's office, Washington, D. C., G. W. Bowman, 1860; Thirty-Sixth United States Congress, First Session, Senate Executive Document, no. 52, Washington, Government Printing Office, 1860, p. 37. Stenn, F.: "Alkali Disease": Selenium Poisoning, Arch. Path. **22**:398, 1936. Franke, K. W.: A New Toxicant Occurring Naturally in Certain Samples of Plant Foodstuffs: 1. Results Obtained in Preliminary Feeding Trials, J. Nutrition **8**:597, 1934. Trelease, S. F.: Bad Earth, Sci. Monthly **54**:12, 1942. Dudley, H. C.: Selenium as a Potential Industrial Hazard, Pub. Health Rep. **53**:281, 1938. Motley, H. L.; Elles, M. M., and Ellis, M. D.: Acute Sore Throats Following Exposure to Selenium, J. A. M. A. **109**:1718 (Nov. 20) 1937. Moxon, A. L., and Rhian, M.: Selenium Poisoning, Physiol. Rev. **23**:305, 1943.

2. Dudley, H. C.: Toxicology of Selenium: V. Toxic and Vesicant Properties of Selenium Oxychloride, Pub. Health Rep. **53**:94, 1938. Lauer, D. J.: Selenium Poisoning, Monograph, Pittsburgh, University of Pittsburgh, 1938.

many of the more stable inorganic compounds which might be used as therapeutic agents in topical therapy.

MATERIALS

A moderately stable preparation of selenium disufide was accepted tentatively for therapeutic use and study, in the form of a shampoo having the following approximate composition:

	Per Cent
Selenium disulfide	2.5
A nacconol® surface-active agent (NRSF)	17.0
Inert and stabilizing ingredients	5.2
Water, sufficient to make	100.0

Before clinical observations were undertaken it was necessary to know the toxic potentialities of this shampoo and certain of its components with respect to the extent, if any, of their absorption through intact skin. A preliminary investigation of this type was undertaken by others in the Kettering Laboratory in the Department of Preventive Medicine and Industrial Health, in which animals were employed at first, after which further observations were carried out on a small number of human volunteers. The results indicated that the shampoo could be employed without risk under appropriate conditions, and, therefore, more elaborate tests could be carried out on a large number of persons.

IRRITATION AND SENSITIZATION

Human subjects were subjected to single and repetitive cutaneous patch tests in an effort to examine the irritant and sensitizing properties of the shampoo in its entirety and of its individual constituents. Thereafter, some of these and other subjects were exposed to more prolonged and more frequently repeated contact with the shampoo, in order to bring out any undesirable reactions and also to determine the therapeutic efficacy of the compound when used in the treatment of seborrheic dermatitis.

The series of patch tests were performed on 100 apparently normal persons. The results of these tests were observed and recorded after 24 and 48 hours. The test was repeated on the same area of the skin of each of the subjects at weekly intervals for four weeks, to detect any evidence of sensitization.

The whole shampoo was used in the first series of individual and repetitive tests on the group of 100 persons without inducing a positive reaction in any instance.

The undiluted individual constituents of the shampoo, including the selenium compound in the form of a powder, were then applied in 48-hour patch tests on the skin of the same persons who had been treated with the whole shampoo. No positive reactions were observed.

ABSORPTION AND EXCRETION OF SELENIUM UNDER VARYING CONDITIONS OF THE USE OF THE EXPERIMENTAL SHAMPOO

Investigations on the absorption, distribution and excretion of selenium have indicated that selenium is chiefly eliminated in the urine.[3]

3. Dudley, H. G.: Toxicology of Selenium: Study of Distribution of Selenium in Acute and Chronic Cases of Selenium Poisoning, Am. J. Hyg. **23**:169, 1936. McConnell, K. P.: Distribution and Excretion Studies in the Rat After a Single Subcutaneous Injection of Sodium Selenium Containing Radio Selenium, J. Biol. Chem. **141**:427, 1941.

Accordingly, observations were made to determine the rate of the urinary excretion of selenium on the part of certain human subjects before and after the use of the shampoo. The method employed for the determination of the selenium in the urine specimens was the one described by Klein.[4] Klein's method gave no details for the preparation of urine samples. His procedure for the preparation of dried grape fruit rind samples was, however, employed for the preparation of approximately 200 ml. of urine for analysis.

1. Nineteen patients with frankly diseased scalps were selected from the 90 persons with seborrheic dermatitis who were being treated with the shampoo. These patients used the shampoo at home, observing no special precaution other than the directions for shampooing the hair. Each patient was required to collect a "spot" sample of his urine prior to the use of the shampoo and a 24-hour specimen

TABLE 1.—*Concentration of Selenium in the Urine of Patients Before and After the Use of a Shampoo Containing a Selenium Compound in the Therapy of Seborrheic Dermatitis*

Patient's Age, Race, Sex	Preshampoo Mg. of Selenium per Liter	Postshampoo Mg. of Selenium per Liter	Difference in Selenium Concentration	Duration of Disease	Sites of Involvement
40, W, F	0.009	0.055	+ 0.046	10 years	Ears, face, scalp, forehead
65, W, M	0.050	0.052	+ 0.002	20 years	Forehead, scalp
61, W, F	0.032	0.071	+ 0.039	15 years	Scalp, with severe generalized dermatitis
38, W, M	0.054	0.114	+ 0.060	5 years	Scalp
17, N, F	0.059	0.051	— 0.008	4 years	Scalp
39, N, F	0.036	0.056	+ 0.020	10 years	Scalp, forehead
38, W, F	0.070	0.015	— 0.055	15 years	Scalp, ears, face, axillas
25, W, F	0.031	0.055	+ 0.024	4 years	Scalp
43, W, F	0.074	0.127	+ 0.053	5 years	Scalp
33, W, F	0.080	0.017	— 0.063	6 years	Scalp
33, N, F	0.066	0.055	— 0.011	4 years	Scalp
37, W, M	0.054	0.068	+ 0.014	20 years	Scalp
28, N, F	0.13	0.13	0	1 month	Scalp
23, W, F	0.017	0.100	+ 0.093	5 years	Scalp
23, M, F	0.081	0.080	— 0.001	1 year	Scalp
24, W, M	0.027	0.024	— 0.003	3 months	Scalp
24, W, M	0.11	0.11	0	1 year	Scalp
9, W, M	0.120	0.055	— 0.065	3 months	Scalp
24, W, M	0.046	0.085	+ 0.039	10 years	Scalp

after its use. Instructions were given for the avoidance of contamination of the urine with the shampoo which might remain on the hands. Chemically clean glass containers were supplied to each patient. The results of these analyses are given in table 1.

The concentrations of selenium in the "spot" samples of the urine of two of the patients, just before their use of the shampoo, may be seen to be the same as those found in the urine voided by the corresponding patients during the period of 24 hours after the use of the shampoo. In seven other instances, the 24-hour sample obtained after the use of the shampoo was lower in its concentration of selenium than was the preapplication sample. Ten of the postapplication samples of urine yielded results which ranged from 0.002 to 0.093 mg. of selenium per liter higher than the corresponding preapplication samples; the differences were less than 50

4. Klein, A. K.: Report on Selenium, J. Assoc. Off. Agr. Chemists **26**:346, 1943.

micrograms in seven of the 10. The highest concentration of selenium found in the urine of these patients was 0.13 mg. per liter, a value which was obtained in the initial sample before the use of the shampoo and also in the 24-hour sample (post-application) of patient R. B.

The entire range of the analytical results on both series of the samples of the urine of these 19 patients, when expressed in the comparable terms of concentration (0.009 to 0.130 mg. of selenium per liter of urine), was practically the same as that found previously in the Kettering Laboratory on the analysis of 57 samples of the urine of 22 normal, healthy persons whose exposure to selenium was of the incidental and apparently unavoidable type associated with their dietary habits while residing in an area of which the soil is not seleniferous (0.012 to 0.11 mg. of selenium per liter of urine). It is apparent, therefore, that to the extent that the

TABLE 2.—*Selenium Content of Successive Twenty-Four Hour Samples of the Urine of Patient D. S. While Under Treatment with a Shampoo Containing Selenium Disulfide*

Date	Volume of Urine, Ml.	Concentration, Mg. of Selenium per Liter	Total Selenium in 24 Hours, Micrograms
12-10-48	1,510	0.060	90.6
12-11-48	790	0.043	34.0
12-12-48	1,260	0.063	79.4
12-13-48	740	0.004	2.96
12-14-48	800	0.052	41.6
12-16-48	1,280	0.077	98.7
12-17-48	1,940	0.078	151.3
12-18-48	1,200	0.088	110.0
12-20-48	1,580	0.071	43.6
12-21-48	1,250	0.088	131.2
12-22-48	890	0.049	43.6
12-23-48	1,620	0.081	131.2
12-24-48	1,080	0.059	63.7
12-25-48	810	0.065	52.7
12-26-48	780	0.026	20.3
12-27-48	930	0.070	51.1
12-28-48	1,500	0.065	97.5
12-29-48	540	0.065	35.1
12-30-48	940	0.056	52.7
Average	1,128	0.061	72.3

urinary excretion of selenium is indicative of the rate and/or the extent of the current absorption of selenium on the part of the subjects, the patients employed in these observations did not absorb any significant increment of selenium as the result of their use of the selenium-containing shampoo.

2. In order to investigate the possibility that selenium might be absorbed when large, discontinuous, denuded and fissured surfaces of the scalp were exposed to the shampoo on successive days over considerable periods, two persons with very severe cases of atopic dermatitis, in addition to the 19 referred to above, were studied individually. Nurses carried out the mechanics of the shampooing in each case so as to limit variability in the technique of the procedure. For the period of 19 consecutive days in one case and of 14 consecutive days in the other, a shampoo was given daily between 10 a. m. and 12 noon and specimens of urine were collected from 8 a. m. of each day until 8 a. m. of the next.

The results obtained by the analysis of the urine of these patients are given in detail in tables 2 and 3. One of these patients displayed an equivocal trend

toward increase in the urinary excretion of selenium during the experiment, but there was no corresponding trend in the other instance. In neither case was there any sustained increase in the urinary concentration of selenium above levels which have been found in the urine of normal healthy persons whose exposure to selenium was limited to contact with that present in generally available foods and beverages.

CLINICAL OBSERVATIONS

Method of Application.—The experimental shampoo was employed therapeutically in 90 cases of seborrheic dermatitis of the scalp and 14 cases of scaling dermatoses including atopic dermatitis, tinea capitis and exfoliative dermatitis.

The cases of seborrheic dermatitis were classified into the four following groups for the purpose of clinical study on the basis of the criteria indicated:

(1) Severe—cases in which the entire scalp was involved and the condition uncontrolled by any amount of shampooing with common detergents

TABLE 3.—*Selenium Content of Successive Twenty-Four Hour Samples of the Urine of Patient E. V. While Under Treatment with a Shampoo Containing Selenium Disulfide*

Date	Volume of Urine, Ml.	Concentration, Mg. of Selenium per Liter	Total Selenium in 24 Hours, Micrograms
12-26-48	140	0.050	7.0 (preshampoo)
12-27-48	920	0.045	41.4
12-28-48	530	0.055	29.1
12-29-48	680	0.005	3.4
12-30-48	800	0.085	73.0
12-31-48	400	0.120	36.0
1- 1-49	500	0.070	35.0
1- 2-49	860	0.080	68.8
1- 3-49	1,080	0.030	32.4
1- 4-49	1,860	0.085	158.1
1- 5-49	860	0.080	68.8
1- 6-49	1,020	0.105	107.1
1- 7-49	900	0.170	153.0
1- 8-49	570	0.150	85.5
1- 9-49	1,260	0.080	100.4
1-11-49	1,220	0.075	91.6
Average	853.7	0.080	67.55

(2) Moderate—cases in which the amount of scaling, erythema, seborrhea, flaking and subjective sensations could be reduced but not controlled completely with a shampoo of ordinary detergents employed two to three times weekly

(3) Mild—persistent cases of dry or oily seborrhea without erythema which could be fairly well controlled by regular shampooing, twice weekly with ordinary detergents

(4) Scalp and glabrous involvement—cases which exhibited varying degrees of seborrheic dermatitis of the scalp with concomitant seborrheic lesions elsewhere on the body

Directions for shampooing were given to each patient as follows:

1. Wet head thoroughly with warm water.
2. Apply 1 to 2 teaspoons (4 to 10 ml.) of shampoo and work into scalp until lather is obtained.
3. Rinse, and repeat process.
4. Allow shampoo to remain in contact with scalp for a minimum of five minutes.

5. Rinse scalp thoroughly by using at least six changes of water or by showering with running water for five minutes.

Although the severity of involvement varied considerably in this group of cases the same routine was prescribed in each—two shampoos weekly for two weeks, followed by one shampoo weekly for the remainder of the period of observation.

Control Procedure.—In setting up the clinical experiment it became apparent that, because of the uncontrollable variables which alter the course of the disease in any one subject, a separate group of control subjects was not justified. Instead, the detailed history of each subject, with respect to the results of prior usage of detergents, shampoos and medicaments, served as control data.

Observations.—The 90 persons with seborrheic dermatitis in this clinical study were treated and observed for a period ranging from one to seven months. No other therapies or detergents were employed during the test period in which the experimental shampoo was in use. In practically all the cases in this group various detergents, shampoos, hair tonics and medicaments had been employed previously. During the test period clinical observations were made in each case and interpreted in the terms indicated below, according to more or less arbitrary criteria.

(1) Complete control—absence of symptoms of pruritus or burning sensations and disappearance of all objective evidence of desquamation and erythema

(2) Moderate improvement—some existing evidence of the disease but no subjective complaints, e. g., itching and burning

(3) Mild improvement—subjective improvement but with persistent signs of active seborrheic flaking and erythema

(4) No change

(5) Definite extension of the disease

(6) Irritation—evidence by eczematization of the involved areas without definite extension of the primary disease process

Results.—An inspection of the skin and scalp of all patients was made biweekly by a single observer. Of the cases of seborrheic dermatitis, 81.1 per cent were completely controlled during the period in which the shampoo was used, 13.3 per cent were improved, 4.4 per cent showed only slight improvement and 1.1 per cent gave no evidence of change.

In the majority of cases the subjective complaints (itching and burning) were alleviated after the second or third shampoo and the objective improvement was evident after the first to second week of treatment. In those cases in which, eventually, complete control was achieved the optimum results were obtained between the fourth and eighth week of treatment.

The best results were obtained in the mildest type of seborrhea of the scalp, e. g., common dandruff. All the cases of this condition showed pronounced improvement after two to four weeks of treatment. Of this group 95.4 per cent were completely controlled.

The largest group was comprised of cases of moderate severity. Of the 39 cases in this group, 33 (84.6 per cent) were controlled completely by the shampoo and five (12.8 per cent) showed definite signs of improvement.

The lowest percentage of complete control (57 per cent) occurred in cases in which the dermatitis extended on to the nonhairy skin of the forehead, face, chest and back. However, it was observed that when such cases responded to treatment the involvement of the glabrous skin subsided rapidly after the scalp had cleared.

Several times during the period of the observations the supply of the shampoo was exhausted and was not renewed for some weeks. During these periods more than 20 patients whose condition had responded partially or completely to treatment with the experimental shampoo were kept under observation for three to five weeks without further resort to such treatment. In some cases the disease could be controlled adequately through the use of various other commercially prepared shampoos, but in others there was exacerbation of the seborrheic disease. This usually became evident two to three weeks after the use of the experimental shampoo had been discontinued. After a new supply had been received and these patients had renewed its use, their signs and symptoms disappeared again within one to two weeks.

TABLE 4.—*Summary of Results Obtained in the Therapy of Seborrheic Dermatitis by the Use of the Experimental Shampoo* *

Classification of Cases	No. of Cases	Complete Control		Moderate Improvement		Slight Improvement		Extension or Irritation		No Change	
		No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
Severe	15	11	73.3	2	13.3	1	6.66	0	0	1	6.6
Moderate	39	33	84.6	5	12.8	1	2.6	0	0	0	0
Mild	22	21	95.4	1	4.54	0	0	0	0	0	0
Glabrous	14	8	57.1	4	28.5	2	14.3	0	0	0	0
Totals	90	73	81.1	12	13.3	4	4.4	0	0	1	1.1

* Cases were observed after treatment for periods varying from one to seven months.

TABLE 5.—*Summary of Results Obtained by the Therapeutic Use of the Experimental Shampoo for Severely Desquamating Dermatoses of the Scalp Other than Seborrheic Dermatitis*

Diagnosis	No. of Cases	Complete Control	Improvement		Extension	Irritation	No Change
			Moderate	Slight			
Atopic dermatitis	2	0	2	0	0	0	0
Folliculitis decalvans	1	0	0	0	0	0	1
Tinea capitis	7	0	0	0	0	0	7
Exfoliative dermatitis	3	0	2	1	0	0	0
Tinea amiantacea	1	0	1	0	0	0	0
Totals	14	0	5	1	0	0	8

Among the 14 cases of scaling dermatoses of the scalp which were treated there was a decrease in scaling and pruritus in five cases. However, the disease process persisted in each patient. Seven children with ringworm of the scalp were treated without improvement or change after six to eight weeks. Microsporum audouini was found to be the pathogenic fungus in each of these cases.

The observations are presented numerically in tables 4 and 5.

One hundred and four persons were treated with the shampoo and observed for one to seven months. In no subject was there any evidence of systemic intoxication, local irritation or sensitization.

SUMMARY

The irritant and sensitizing properties of a shampoo containing selenium disulfide were investigated. It was found by 48-hour and repetitive patch tests for four weeks that the active constituent of the shampoo, selenium disulfide, produced neither primary irritation nor sensitization reactions in 100 normal subjects.

The shampoo, containing selenium disulfide, was employed therapeutically, over periods from one to seven months in 104 cases, 90 of which were cases of seborrheic dermatitis, without inducing signs of irritation, sensitization or toxicity.

Eighty-one per cent of the cases of seborrheic dermatitis of all degrees of severity were controlled completely by the use of the shampoo. Ninety-five per cent of the mild and 85 per cent of the moderate cases of this disorder of the skin were controlled completely during the period of use of this shampoo.

The use of the shampoo exerted no influence on the clinical course of seven cases of tinea capitis associated with the presence of M. audouini. Two cases of atopic dermatitis and three cases of exfoliative dermatitis were benefited by the use of the shampoo, in that the amount of scaling of the scalp was reduced thereby.

The use of the shampoo on one occasion, in the usual manner of employing such a material (as described), on the diseased scalp of each of 19 patients did not result in the absorption of selenium to an extent that could be detected on the basis of any regular or significant increase in the excretion of selenium in the urine of the patients.

The use of the shampoo on the badly fissured scalps of two patients for 14 and 19 successive days, respectively, failed to provide definite evidence of initial or progressive absorption of selenium.

Clinical Notes

STREPTOMYCIN THERAPY OF ERYTHEMA INDURATUM

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Since streptomycin was first isolated from Streptomyces griseus, in September 1943, reports have appeared in the medical literature concerning its efficacy in treating various diseases of the skin.[1] Those conditions which have been reported as amenable to streptomycin therapy include lupus vulgaris, scrofuloderma, tuberculosis miliaris disseminata faciei, tuberculous ulcers of the tongue, tuberculosis verrucosa cutis, actinomycosis, tularemia, chancroid, granuloma inguinale and various dermatoses due to Pseudomonas aeruginosa (Bacillus pyocyaneus).[2] A careful search of the literature fails to reveal any reports on the treatment of erythema induratum with this antibiotic, and therefore two cases from the dermatology clinic at the Vanderbilt University Hospital are being recorded.

REPORT OF CASES

CASE 1.—E. M., a 36 year old white housewife, was first seen in October 1945 at the Vanderbilt University clinic. The "glands in her neck" had begun enlarging eight months earlier, and a sudden acute swelling had appeared the preceding month. The glandular enlargement was not accompanied with local heat or fever, and weight loss was not present. The patient had no history of previous serious illness except a ruptured appendix in 1941.

Examination revealed no abnormality except the presence of visibly enlarged lymph nodes on each side of the neck. Laboratory examinations showed normal blood counts, a negative Kahn reaction and normal values on examination of the urine. A node was removed on Nov. 13, 1945 for microscopic section, and the diagnosis was made of tuberculosis of the cervical lymphatics. However, inoculation of gland tissue into a guinea pig did not reveal tuberculosis. A roentgenogram of the chest showed a shadow in the upper lobe of the right lung which was considered to be tuberculous.

In February 1947 an eruption appeared on the posterior surface of both legs which was diagnosed as erythema induratum. Several of the lesions became ulcerated. X-ray therapy was begun, approximately 500 r being given to the involved area, at 100 kv., 5 ma., at 12 inches (30 cm.) distance and with 2 mm. Al filtration. This treatment was given in April and May 1947. All the ulcers slowly healed except a large one on the left calf which seemed resistant to all treatment. In November and December 1947 900 r was given to each side of the neck, the following factors being used: 200 kv., 20 ma., at 50 cm. distance and with 0.5 mm. Cu and 1 mm. Al filtration. This treatment was followed by regression of the cervical nodes, but they did not completely disappear under X-ray therapy. The large ulcer on the left leg showed no sign of healing. On May 17, 1948 streptomycin treatment was begun. Injections of 0.5 Gm. of streptomycin were

From the Division of Dermatology, Department of Medicine, Vanderbilt University School of Medicine.

1. Waksman, S. A.: Streptomycin: Nature and Practical Applications, Baltimore, Williams & Wilkins Company, 1949.

2. Delamater, E. D., in Waksman,[1] pp. 520-523. O'Leary, P. A.; Ceder, E. T.; Hinshaw, H. C., and Feldman, W. H.: Treatment of Various Types of Cutaneous Tuberculosis with Promizole and Streptomycin: Preliminary Report, Arch. Dermat. & Syph. **55**:222-232 (Feb.) 1947. Combes, F. C.; Canizares, O.; Shatin, H., and Kaufman, C.: Streptomycin in Dermatology: Its Value and Limitations, New York J. Med. **48**:2024-2028, 1948.

given twice daily. Complete relief from pain was obtained in three days, and the ulcer began showing signs of improvement. The treatment was continued for 42 days, and healing was complete in 10 months. After three months the cervical nodes were no longer palpable. On a recent visit it was noted that only scars were present to show the location of the previous disease.

CASE 2.—R. A. D., a 16 year old white girl student, was first seen in the clinic on March 6, 1950. According to the history her ankles had been swollen for five weeks. Two weeks before her admission to the clinic an erythematous eruption had appeared bilaterally in the area of the ankles. Approximately one year prior to this date she had had "pleurisy," and recently there had been slight daily elevation of temperature. She neither coughed nor raised sputum. Two of her sisters had been hospitalized with tuberculosis in the past, but their condition was at that time in an arrested state. On examination her temperature was found to be 100.4 F., pulse rate 104 per

Fig. 1 (case 1).—Unhealed ulcer of erythema induration before streptomycin therapy was instituted.

minute, and blood pressure, 130/78. Several purplish lesions were present on the posterior aspect of her legs approximately 3 inches (7.5 cm.) above the ankles. They were firm and indurated. A large tender node was present in the right crural chain of lymph nodes. A roentgenogram of her chest revealed no abnormality, but a tuberculin test elicited a "strongly positive" reaction in a 1 : 1,000 dilution.

The laboratory observations included a white blood cell count of 11,000 and a normal hemoglobin level and differential picture. There were no abnormal urinary observations, and a Kahn test gave a negative reaction. The sedimentation rate was 41 mm. per minute. The electrocardiogram revealed no abnormality. A biopsy was performed on March 24, 1950. The microscopic section was reported to show a picture typical of erythema induratum.

The biopsy wound broke down and would not heal during six weeks of conservative therapy. On May 22, 1950 treatment was begun with a dosage of 1 Gm. of dihydrostreptomycin daily, given in two doses. This was continued for 24 days. The induration had subsided noticeably within

a week from the beginning of treatment and had almost disappeared in two weeks. The ulcer was completely healed after 10 days. Only hyperpigmentation remained at the last examination, on Aug. 23, 1950.

SUMMARY

Two cases are reported of erythema induratum which had not responded well to conventional therapy but healed as the result of treatment with streptomycin. One of the patients had an ulcer for 15 months which had not healed with X-ray therapy and the use of various topical applications. A biopsy wound on the second patient showed no tendency toward healing after two months. The condition in both of these patients underwent dramatic improvement after 42 and 24 days of streptomycin therapy, respectively.

Fig. 2 (case 1).—Healed lesion two years later.

It is interesting to note that the patient in case 1 had a tuberculous cervical adenitis at the time the erythema induratum appeared. A lesion of the lung was strongly suspected by the radiologist as being tuberculous. However this suspicion was never proved. Roentgenologic examination of the chest revealed no abnormality in the second patient although a skin test evinced a strongly positive reaction to tuberculin. A slight afternoon fever, malaise and history of pleurisy had been present for one year.

CONCLUSION

Two cases of erythema induratum are presented, both showing dramatic improvement after a course of streptomycin therapy. No previously reported cases of erythema induratum treated by streptomycin could be found in the literature.

Dr. R. H. Kampmeier assisted in the medical treatment of these cases.

CONTACT DERMATITIS DUE TO CINNAMON

Recurrence of Dermatitis Following Oral Administration of Cinnamon Oil

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Dermatitis due to cinnamon oil is either a rare event or one rarely reported. Only six references to dermatitis from cinnamon or cinnamon oil have been found. White[1] attributed a dermatitis of the hands, face and abdomen of a young woman to cinnamon (cassia) oil used to flavor toothpicks. Tulipan[2] obtained positive reactions to patch tests with cinnamon and cinnamon sugar in a baker with dermatitis of the hands. Silvers[3] reported a case of stomatitis and dermatitis due to sensitivity to clove oil and cinnamon oil. Miller[4] observed cheilitis in a woman exposed to the vapor of cinnamon oil; a patch test with a 2 per cent alcoholic solution of cinnamon oil gave strongly positive reactions, and a fume test with a 1 per cent alcoholic solution of the oil also gave a strong reaction on the forearm in seven hours. Howell,[5] in a tabulation of proved cases of contact dermatitis, mentioned one instance, in a baker, of dermatitis of the hands due to cinnamon. Downing[6] published the photograph of a candy maker with dermatitis of the hands due to cinnamon oil and stated that the patch test evoked a generalized dermatitis.

I am reporting the present case not only because of the apparent rarity of this sensitivity but also because of the following more interesting features. The accidental discovery of the sensitivity to cinnamon oil led to the elucidation of an obscure eczema of the hands of five years' duration. Then, despite repeated contact of the oil with the mucous membrane of the lip and mouth these surfaces remained clinically exempt from the sensitization. And, finally, ingestion of cinnamon and cinnamon oil appeared to activate the eczema of the hands.

REPORT OF A CASE

The patient was a 36 year old white woman who first manifested an itching, blistery rash of the hands in 1945. This eruption persisted throughout the succeeding five years, with variable periods of remission that followed treatment or occurred spontaneously. In November 1949 the patient acquired an itching eruption of the face, presternal region and right forearm, and coincidentally the rash of the hands became worse. This diffuse eruption continued, with little tendency to improvement, until the patient consulted me on March 31, 1950.

There was a subacute dermatitis of the lids of the left eye, the cheeks, the chin, the presternal region and the right forearm, the skin being reddened and edematous but not vesiculated. There was an erythematous vesicular dermatitis of the dorsa of the digits of both hands with considerable redness and puffiness of the eponychias. The palmar surfaces were almost completely free of eruption. The right hand was most severely affected. The lips and buccal mucous membranes were normal.

It was learned that the patient had begun to use a new tooth paste shortly before the onset of the rash of the face, chest and forearm. She was advised to discontinue the use of tooth pastes, and bland topical treatment was prescribed. The dermatitis improved rapidly, and in about five weeks all areas, including the hands, were clear.

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1. White, C. J.: Boston M. J., 1879, cited in White, R. P.: The Dermatergoses or Occupational Affections of the Skin, the Trade Processes, the Responsible Agents and Their Actions, ed. 4, London, H. K. Lewis & Co., Ltd., 1934, p. 442.

2. Tulipan, L.: Dermatitis from Cinnamon, Arch. Dermat. & Syph. **25**:921 (May) 1932.

3. Silvers, S. H.: Stomatitis and Dermatitis Venenata with Purpura, Resulting from Oil of Cloves and Oil of Cassia, Dental Items of Interest **61**:649 (July) 1939.

4. Miller, J. Cheilitis from Sensitivity to Oil of Cinnamon Present in Bubble Gum, J. A. M. A. **116**:131 (Jan. 11) 1941.

5. Howell, J. B.: Contact Dermatitis: An Analysis or Tabulation of All Cases Proved in a Single Year, Arch. Dermat. & Syph. **53**:265 (March) 1946.

6. Downing, J. G.: Occupational Dermatoses (Ergodermatoses): Diagnosis, Disability and Treatment, New England J. Med. **237**:755 (Nov. 20) 1947.

INVESTIGATIONS

A patch test was made with the suspected tooth paste, and this provoked an intensely vesicular reaction. The manufacturer [7] informed me that the tooth paste contained the following ingredients: urea, dibasic ammonium phosphate, tricalcium phosphate, glycerin, sodium lauryl sulfoacetate, a chlorhydroxyphenyl derivative, peppermint oil, methyl salicylate, anise oil, and (cassia) cinnamon oil. Results of patch tests with six ingredients are given in the accompanying table.

The patient was asked to handle cinnamon powder, which she had used a good deal as a flavor, and she noted that brief contact caused her hands to itch, although no eruption was produced.

During the last week of July she ate a piece of cinnamon toast (fed to her by her husband so that there was no contact with her hands), and about eight hours later she had itching of the hands, although no eruption appeared.

On Sept. 28, 1950, just before bedtime, the patient swallowed two capsules containing a total of 0.4 cc. of cinnamon oil. There was no reaction until October 3, five days later, when her hands began to itch intensely. The following day a vesicular eruption appeared on the previously affected digits of the hands, but there was no involvement of the face, presternal region or forearm, and no flare occurred at the patch test site.

Results of Patch Tests

Substance	Reaction
Peppermint oil (1% in alcohol)	Negative
Peppermint oil (25% in castor oil)	Negative
Methyl salicylate (1% in alcohol)	Negative
Methyl salicylate (2% in olive oil)	Negative
Anise oil (1% in alcohol)	Negative
Anise oil (25% in castor oil)	Negative
Cinnamon oil (1% in alcohol)	4+
Sodium lauryl sulfoacetate (1.5% in water)	Negative
Chlorhydroxyphenyl derivative (1.5% in alcohol)	Negative

At 10:15 p. m. on October 18 the patient ingested 15 cc. of tincture of cinnamon (containing 1.5 cc. of cinnamon oil), and about 12 hours later she had itching of the hands and a few blisters. Once again, however, none of the other sites was affected, and the patch test area did not flare.

COMMENT

It is a reasonable assumption that my patient originally became sensitized to cinnamon oil more than five years ago, as a result of repeated contact with cinnamon powder. This sensitization produced the obscure, persistent, refractory eczema of the hands the cause of which eluded detection until the patient chanced to use a tooth paste flavored with cinnamon oil and manifested a more recognizable dermatitis.

The fact that the tooth paste did not provoke cheilitis or stomatitis is not remarkable. Jadassohn [8] pointed out the relative immunity of the mucous membranes in eczematous contact type dermatitis, in the well known case of the woman who acquired severe dermatitis of the labia and thighs from contact with iodoform packing inserted into the vagina, while the vaginal mucosa remained entirely normal.

There are three possible variants of cutaneous and/or mucosal sensitization:

First, there is sensitization of the skin but not of the mucous membranes. This is the commonest variant and is exemplified by the cited case of Jadassohn [8] and the one I am reporting.

7. The manufacturer provided the ingredients for patch testing but requested that the name of the tooth paste be omitted from this report.

8. Jadassohn, J.: Zur Kenntnis der medicamentösen Dermatosen, Verhandl. d. deutsch. dermat. Gesellsch. **5**:103, 1895.

Second is sensitization of the skin and of the mucous membranes. This appears to be an uncommon event. Loveman[9] described a patient with dermatitis of the hand and stomatitis caused by anise oil in a denture cream. Templeton and Lunsford[10] reported cases of cheilitis and stomatitis due to hexylresorcinol tooth paste, in which patch tests with the tooth paste gave positive reactions. Shelmire[11] obtained positive reactions on the tongue and palate with a 1:10 dilution of poison ivy oleoresin in the cases of several patients with cutaneous sensitivity to the weed. Shelmire is "convinced that sensitization to an external agent is always general, the skin and mucous membrane alike being involved. The difference in sensitization of different areas of both skin and mucous membranes is relative." Goldman and Goldman[12] recorded 10 instances of contact stomatitis from tooth paste, plate cleaner, lavender oil, cashew nut oil, mercury, pecans and tobacco, and in seven of these cases cutaneous patch tests gave positive reactions.

The third variant consists in sensitization of the mucous membranes but not of the skin. This seems to be the rarest form of sensitization. Goldman and Farrington[13] reported a case in which stomatitis and glossitis followed ingestion of penicillin tablets and cutaneous patch tests with penicillin gave negative reactions.

Apparently, when the skin is the original surface sensitized the mucous membranes seldom participate in the sensitization on a clinical level. Contrariwise, when the mucous membrane is the original surface sensitized the skin almost always shares in the sensitization, its participation being manifested by clinical dermatitis or by positive reactions to patch tests. The difference in the effects on the two surfaces may be only relative, as suggested by Shelmire,[11] and it is possible that the presence of sensitivity of the mucous membranes could be shown in cases where it appears to be absent were much higher concentrations of allergen employed in testing. The greater refractoriness of the mucous membrane to sensitization may be due to the absence of a keratin layer containing specific proteins that more readily couple with simple chemical compounds to form allergens.

The elicitation of itching on one occasion and of itching and eruption on two other occasions after the ingestion of cinnamon or cinnamon oil is a provocative observation. There have been a number of recent publications[14] dealing with allergy to foods as a cause of recurrent or persistent vesicular eruptions of the hands. In all these the determination of food sensitivity has rested on the use of elimination diets, with improvement of the eruption after elimination of the offending foods and aggravation after their ingestion. In discussing the paper of Livingood and Pillsbury,[14e] Osborne pointed out that foods are highly complex substances, that oleoresins are contained in many foods and "that specific hypersensitivity does exist to the oleoresins in many fruits and vegetables, both from local contact and, in recurrences following this, from the

9. Loveman, A. B.: Stomatitis Venenata: Report of a Case of Sensitivity of the Mucous Membranes and the Skin to Oil of Anise, Arch. Dermat. & Syph. **37**:70 (Jan.) 1938.

10. Templeton, H. J., and Lunsford, C. J.: Cheilitis and Stomatitis from ST 37 Tooth Paste, Arch. Dermat. & Syph. **25**:439 (March) 1932.

11. Shelmire, B.: Contact Dermatitis from Weeds: Patch Testing with Their Oleoresins, J. A. M. A. **113**:1085 (Sept. 16) 1939.

12. Goldman, L., and Goldman, B.: Contact Testing of the Buccal Mucous Membrane for Stomatitis Venenata, Arch. Dermat. & Syph. **50**:79 (Aug.) 1944.

13. Goldman, L., and Farrington, J.: Stomatitis with Glossitis Following Oral Therapy with Penicillin Tablets, Arch. Dermat. & Syph. **57**:399 (March, pt. 1) 1948.

14. (*a*) Flood, J. M., and Perry, D. J.: Recurrent Vesicular Eruption of the Hands Due to Food Allergy, J. Invest. Dermat. **7**:309 (Dec.) 1946. (*b*) Rowe, A. H.: Atopic Dermatitis of the Hands Due to Food Allergy, Arch. Dermat. & Syph. **54**:683 (Dec.) 1946. (*c*) Flood, J. M., and Perry, D. J.: Role of Food Allergy in Eczematoid Dermatitis, ibid. **55**:493 (April) 1947. (*d*) Winston, B. H., and Sutton, R. L., Jr.: Dermatitis of the Hands Due to Ingested Allergens, ibid. **58**:335 (Sept.) 1948. (*e*) Livingwood, C. S., and Pillsbury, D. M.: Specific Sensitivity to Foods as a Factor in Various Types of Eczematous Dermatitis, ibid. **60**:1090 (Dec.) 1949.

ingestion of the specific oleoresin." In discussing the same paper, Sulzberger emphasized the fact that many foods are conveyed to the mouth by the hands and that contact exacerbation of eczematous dermatitis by such means must be excluded.

The case reported here exemplifies the possibility that certain simple chemical components of foods, not protein sustances, may produce contact dermatitis of the hands, which in turn may be exacerbated and perpetuated by the ingestion of the responsible food. That this may be more widespread an occurrence than realized is suggested by the long list of foods collected by Weber [15] as reported causes of contact type dermatitis (garlic, allspice, artichokes, asparagus, barley, corn oil, figs, grapes, lemon juice and lettuce, among others).

SUMMARY

A proved case of sensitivity to cinnamon oil is reported.

Elicitation of a distinctive dermatitis due to tooth paste flavored with cinnamon oil led to clarification of a chronic vesicular dermatitis of the hands of five years' duration. The hand eruption had occurred first and had apparently been induced by repeated contact with cinnamon powder.

Patch tests with cinnamon oil, 1 per cent in alcohol, gave a 4 + reaction.

Cure of the entire eruption followed cessation of contact with cinnamon.

The lips and buccal mucous membrane did not participate in the clinical sensitization; the implications of this observation are discussed.

Ingestion of cinnamon powder was followed by itching of the hands in 12 hours. Ingestion of cinnamon oil was followed by itching and vesiculation of the hands after five days (delayed reaction) on one occasion and after 12 hours on a second occasion. The implications of this observation in relation to chronic eczema of the hands are discussed.

10 East Seventy-eighth Street (21).

15. Weber, L. F.: External Causes of Dermatitis, Arch. Dermat. & Syph. **35**:129 (Jan.) 1937.

FURTHER CLINICAL OBSERVATIONS ON SEABATHER'S ERUPTION

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During the last two years I have observed two epidemics of seabather's eruption [1] at Guantanamo Bay, Cuba. The cases appeared spasmodically from April to September in 1949 and 1950. Local fishermen have been aware of this condition for years during the above-mentioned season. Fifty-seven cases which resembled very closely the cutaneous eruption described by Sams as "seabather's eruption"were seen in consultation.

The eruption, which consists of erythematous, mostly perifollicular pruritic papules with centrally crusted puncta, is located on the flexure and covered surfaces. The history and the location of the eruption help to differentiate this condition from the dermatitides caused by Portuguese man-of-war, hydroids, coral, cercaria of schistosomes and bites of the different classes of arthropods.

As far as the etiological agent is concerned, I have nothing definite to offer. Macroscopic and microscopic studies of samples of seawater taken from the five available beaches revealed nothing unusual. There was no gross change in the color or character of the water. No unusual marine life or vegetation was seen at the beaches. There was no invasion of the beaches by living or dead jellyfishes or sessile polyps. A personal communication from Sams revealed that the schistosomes are presently being investigated as the possible etiological agent.

The opinions expressed in this article are those of the author and are not to be construed as reflecting those of the Navy or the Navy Medical Department.

1. Sams, W. M.: Seabather's Eruption, Arch. Dermat. & Syph. **60**:227-237 (Aug.) 1949.

A typical case history usually ran as follows: After swimming in the sea for about five minutes, the patient felt many stings. About four or five hours later he manifested a red, itching papular eruption in the flexure and bathing suit areas. Some 12 to 14 hours later, if the involvement was extensive, he experienced fever, chills, nausea and vomiting. The eruption involuted spontaneously within 10 to 20 days.

Although the eruption in the cases I observed resembled Sams' morphologically, some of these cases presented clinical differences worthy of mention. With the onset of an extensive eruption, six patients acquired a nonpurulent conjunctivitis, which cleared within two days without any therapy. Systemic manifestations were seen not only in children but also in adults who had extensive cutaneous involvement. Ten adults and two children were seen with a temperature of 102 F. and above, chills, headache, nausea and nonprojectile vomiting. These "toxic" systemic reactions lasted for 24 to 72 hours. The physical examinations and laboratory studies revealed no potential cause for these systemic reactions other than the dermatitis. In five cases the eruption did not appear until four to five days after the exposure. In nine patients, who had no further exposures or complicating dermatoses, there was an extension of the primary eruption three to six days after its onset.

Some laboratory work was done on the persons who manifested the systemic reactions. The white blood cell count revealed slight leukocytosis with a very slight shift to the left. There was no eosinophilia or toxic changes in the white blood cells. The urinalyses revealed no abnormality. The blood Kahn tests gave negative reactions. The blood sedimentation rates (Cutler method), which were determined in only three cases, were within normal limits.

The eruption was treated symptomatically with a modified calamine lotion applied locally, diphenhydramine (benadryl®) hydrochloride given in doses of 50 to 100 mg. four times daily by mouth and calcium gluconate administered intravenously in 10 to 20 cc. doses daily. The above routine was adequate for the average cases but failed to control the pruritus in the cases with more extensive involvements.

COMMENTS

Sams' seabather's eruption is a definite dermatological entity which can cause "toxic" systemic reactions if there is sufficient cutaneous involvement. Children seem prone to acquire a more extensive cutaneous eruption. This fact plus the tendency for children to play in shallow water suggests the possibility that the offending agent is more concentrated in these shallow waters. Several patients volunteered the information that their eruption appeared when the tide was coming in. A few of the base personnel believed that they aborted an attack by immediately showering themselves with plenty of soap and water and then rubbing themselves down with alcohol. The delay of a few days before the appearance of the eruption and the extension of the eruption a few days after its onset raises the possibility of a sensitivity phenomenon similar to that seen in parasitic infections, e. g., scabies. The laboratory studies in the severer cases revealed nothing significant. Palliative therapy was relatively effective. The evidence seems to point to a living, free floating organism, which is capable of stinging, as the responsible agent.

ACRODERMATITIS PUSTULOSA PERSTANS: A METHOD OF TREATMENT

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Acrodermatitis pustulosa perstans has, since its recognition, been a most interesting and baffling skin disorder to treat. The above name, given by Sachs, MacKee and Rothstein,[1] emphasizes the persistency of the disease in spite of all usual therapeutic measures. So also does the synonym recalcitrant pustular eruptions of the palms and soles.[2] The diversity in thought

1. Sachs, W.; MacKee, G. M., and Rothstein, M. J.: Acrodermatitis Pustulosa Perstans (So-Called Pustular Psoriasis), Arch. Dermat. & Syph. **56**:766 (Dec.) 1947.

2. Andrews, G. C.; Berkman, F. W., and Kelly, R. J.: Recalcitrant Pustular Eruptions of the Palms and Soles, Arch. Dermat. & Syph. **29**:548 (April) 1934.

as to etiology is emphasized by the other synonyms, namely, pustular psoriasis of Barber [3] and pustular bacterids of Andrews and Machacek.[4] The etiology is still unknown. The histopathological picture is now clear, thanks to Wilbert Sachs.[5]

Recently such unusual success was obtained in clinically clearing consecutive cases of acrodermatitis pustulosa perstans that it was thought worth while to record the method of treatment so that more widespread evaluation might be undertaken.

These cases showed the typical clinical appearance of tiny, deep vesiculopustules studding erythematous, slightly scaly patches on the palms and soles. Biopsies showed the histopathological picture to be that of a large pustule in the prickle cell layer, filled with polymorphonuclear leukocytes and cellular debris. There was no spongiosis near the pustule and only little acanthosis. There was no thinning of the suprapapillary plates and no elongation or clubbing of the rete pegs. In the cutis below the pustule there was some small round cell infiltration and occasionally polymorphonuclear leukocytes were found. Cultures and slides were negative for fungi. No patient showed signs of psoriasis elsewhere. No patient knew of any relative having a similar disorder.

Ten consecutive patients with acrodermatitis pustulosa perstans were successfully clinically cleared by the daily oral administration of 150,000 units of vitamin A, the frequent application of 5 per cent coal tar solution in a water-soluble base and the weekly administration of suberythema doses of radiation from a cold quartz lamp.

Three characteristic case studies are presented.

Case 1.—R. H., a 42 year old white married woman, had had typical lesions on the soles for one year. While the patient was treated with radiation from a cold quartz lamp and coal tar solution alone, there was some improvement but soon a plateau was reached. When the administration of 150,000 units of vitamin A daily was added, there was pronounced improvement in one week, and the patient became clinically well in nine weeks. The patient had remained well for several months at the time of writing; she continued to take vitamin A.

Case 2.—F. M., a 56 year old white man, had had typical lesions of the palms for seven years. Intermittent X-ray therapy given elsewhere usually improved the condition but only for a short time. After two weeks of treatment with vitamin A, coal tar solution and radiation from a cold quartz lamp, the condition became clinically clear, and it remained so.

Case 3.—H. S., a 46 year old white physician, had had a typical involvement of the palms for 15 years. On treatment with radiation from a cold quartz lamp and coal tar solution he made moderate improvement, though with frequent flare-ups. When administration of vitamin A was added, pronounced improvement started within one week and the patient became clinically well in 10 weeks. The patient had been well for months at the time of writing and was certain the real improvement started with the addition of vitamin A therapy, which he was continuing.

The plan for the above-described method came about by trial and error and especially because of the failure of the use of sulfonamides and penicillin, the removal of foci of infection, X-ray therapy and other advocated measures to influence the course of the disease other than for a short time. While vitamin A seems to be the major factor in clearing the lesions, a failure of response to vitamin A alone in one patient plus the fact that the coal tar solution preparation makes the patient much more comfortable led me still to use the combination of all three agents.

SUMMARY

A method is described of treating acrodermatitis pustulosa perstans with the oral use of 150,000 units of vitamin A daily, frequent application of 5 per cent coal tar solution in a water-soluble base and weekly suberythema doses of radiation from a cold quartz lamp.

Three typical case histories are presented from a series of 10 consecutive cases in which there was clinical clearing following this method of treatment.

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3. Barber, H. W.: Presentation of Cases of Pustular Psoriasis and Discussion of Same, Brit. J. Dermat. **45**:113 (March) 1933.

4. Andrews, G., and Machacek, G. F.: Pustular Bacterids of the Hands and Feet, Arch. Dermat. & Syph. **32**:837 (Dec.) 1935.

5. Sachs, W., and Scannone, F.: So-Called "Pustular Psoriasis," J. Invest. Dermat. **6**:349 (Dec.) 1945.

GRANULOMA ANNULARE

Dissemination Following Administration of Calciferol

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The therapeutic effectiveness of calciferol in cases of lupus vulgaris reported by Charpy [1] and by Dowling and Thomas [2] has been confirmed by many investigators. In the course of studies on the drug the use of calciferol has been extended to other forms of cutaneous tuberculosis as well as to other eruptions whose relationship to tuberculosis is not completely understood.

Granuloma annulare may be placed in the latter group. Although its relationship to tuberculosis has been suggested in the past, most authorities now agree that, despite the occasional coincidence of tuberculosis elsewhere in the body, the clinical and histopathological observations speak against a tuberculous etiology of granuloma annulare.

Pascher, Silverberg, Marks and Markel [3] reported on five cases of granuloma annulare in their therapeutic assay of calciferol. In discussing their results they stated that widespread dissemination of the lesions occurred in two patients while they were taking calciferol. These cases recently came to our attention again, and since individual case reports [4] in the ARCHIVES indicate an interest in this phenomenon, a report of these cases in more detail seemed indicated.

CASE 1.—S. W., a 57 year old white man, was first seen at the Skin and Cancer Unit on Nov. 6, 1946. He presented a half-dollar-sized circular lesion with a firm, elevated, tortuous periphery and a depressed center, of one year's duration, on the dorsum of the left hand. There was a small pea-sized satellite lesion, and small similar lesions were present on the dorsum of the right hand. Tuberculin tests (old tuberculin Koch) were done on November 5 and repeated on November 13 with identical results, as follows: 1:1,000, + +; 1:10,000, —; 1:100,000, —, and 1:1,000,000, —. A biopsy was performed on November 8, and the histologic diagnosis was granuloma annulare.

Treatment with calciferol was begun on December 27 at a dosage of 50,000 units three times daily. Four weeks after the onset of therapy new lesions were noted on the back of the neck and the lesions on the hands had increased in size. The same dosage of calciferol was continued until Feb. 14, 1947, when therapy was stopped because of the appearance of many new lesions. The lesions continued to spread despite discontinuance of use of the drug and involved the forehead and cheeks, the entire neck and the forearms as well as the dorsa of the hands.

During this period of dissemination of the lesions the patient received eight quarter-skin-units (75 r each) at weekly intervals. On April 14 the patient was given potassium arsenite (Fowler's) solution by mouth, 5 drops twice a day, and this regimen was continued until July 9, when the "new lesions" had disappeared but a few lesions still remained on the dorsum of the left hand. When the patient was seen again, in May 1950, these lesions on the dorsum of the left hand were still present.

From the Department of Dermatology and Syphilology of the New York University Post-Graduate Medical School, Dr. Marion B. Sulzberger, chairman, and the Skin and Cancer Unit of University Hospital.

1. Charpy, J.: Le traitement des tuberculoses cutanées par la vitamine D_2 à hautes doses, Ann. dermat et syph. **6**:310, 1946.

2. Dowling, G. B., and Thomas, E. W. P.: Treatment of Lupus Vulgaris with Calciferol, Clinic J. **75**:180, 1946.

3. Pascher, F.; Silverberg, M. G.; Marks, I. E., and Markel, J.: Therapeutic Assays of the New York Skin and Cancer Unit, Post Graduate Medical School, New York University-Bellevue Medical Center: Assay II—Calciferol (D_2), J. Invest. Dermat. **13**:89, 1949.

4. Hall, F.: Granuloma Annulare, with Dissemination Following Calciferol Therapy, Arch. Dermat. & Syph. **61**:145 (Jan.) 1950. Epstein, N., and Allen, J.: Generalized Granuloma Annulare, ibid. **62**:453 (Sept.) 1950.

CASE 2.—R. R., a white woman 54 years old, was first seen at the Skin and Cancer Unit on Nov. 26, 1946. Characteristic gyrate, papular, confluent, annular plaques, semicircles and discrete papules were present on the dorsa of the hands, more pronounced on the right hand than on the left.

A biopsy was performed on December 3, and a histologic diagnosis of granuloma annulare was made. Tuberculin tests performed on December 17 with old tuberculin Koch were read as follows: 1 : 10,000, + + +; 1 : 100,000, + +, and 1 : 1,000,000, +. Examination of the urine, a complete blood count and the serologic picture showed no abnormality.

On Jan. 21, 1947 calciferol therapy was instituted, with 240,000 units daily for six days, after which time the dose was reduced to 150,000 units daily until February 25, when it was reduced to 75,000 units daily; treatment was discontinued April 4. New lesions were noted three weeks after treatment was begun, first on the dorsa of the hands and fingers, then on the forehead (February 25) and then generalized over the trunk, neck, shoulders, upper and lower extremities and on the forehead (April 4). A second biopsy was performed, on a lesion above the left clavicle, on April 22, and reported as showing granuloma annulare.

Most of the widespread lesions had cleared by May 27, and when the patient was last seen, later in the year, she stated that they had all cleared by July without further therapy.

Two cases of granuloma annulare which apparently underwent dissemination after calciferol therapy are reported. Dissemination does not occur in every case of granuloma annulare treated with calciferol. It may be stated, however, that calciferol not only is ineffective in this condition but also appears to aggravate the lesions in some cases.

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ATROPHIA MACULOSA VARIOLIFORMIS CUTIS

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Heidingsfeld [1] in 1918 reported the case of a 20 year old white man who presented numerous "pit marks" on his face. These were indistinguishable from the scars seen following variola. The patient denied having had any previous eruption which might account for the marks, or pits. Further questioning of the patient and his immediate family convinced Heidingsfeld that the atrophic areas had appeared spontaneously. The patient's cheeks were studded with sharply defined, shallow, pitted scars. Most of the lesions were round; a few were linear or rectangular, but all were devoid of any inflammatory or pigmentary changes. However, Heidingsfeld described a little erythema and scaling preceding the appearance of the pitted scars. This erythema disappeared quickly, to be followed by atrophy, with occasionally a very faint, residual furfuraceous scaling. Heidingsfeld described this as a new disease to be classed with the so-called spontaneous or idiopathic atrophies of the skin.

Senear [2] presented a similar case in 1923, that of a young woman 18 years of age. The pitted scars were present on the cheeks and forehead. However, the erythema and scaling preceding the lesions, as described by Heidingsfeld, were not present in Senear's case. Unlike the original case described, this case was associated with moderate acne, but Senear did not believe that this involved areas affected by the scarring.

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1. Heidingsfeld, M. L.: Atrophia Maculosa Varioliformis Cutis, J. Cutan. Dis. **36**:285 (May) 1918.

2. Senear, F. E.: A Case for Diagnosis, Arch. Dermat. & Syph. **7**:405 (March) 1923.

REPORT OF A CASE

Mrs. S. B., a 37 year old white woman, first noted "pits" on her face in August 1949. There was no history of any preceding eruption, and the patient had always been proud of her very clear complexion. When first seen for this complaint, in November 1949, the patient presented two or three sharply defined, shallow atrophic scars on her cheeks. These were best seen with side lighting, as had been noted previously by Heidingsfeld. One of the lesions was linear. There was very slight scaling in the center of the lesions. There was no acne, and the rest of the skin was completely clear.

The patient continued to manifest new pitted scars. Figures 1 and 2 indicate the appearance of the lesions on May 31, 1950.

Fig. 1.—A portion of the right side of the face of Mrs. S. B., photographed with side lighting. Note the varioliform scars.

Fig. 2.—A view of the left side of the face of Mrs. S. B., with side lighting. Note the linear scars.

At various times minute areas of erythema with furfuraceous scaling were observed preceding the atrophic lesions. These were recognized by the patient from the beginning as being incipient lesions. There were no accompanying subjective symptoms. The patient's general health had been excellent except that she had had uterine fibroids which had necessitated a hysterectomy in 1947.

No apple jelly nodules were noted on diascopic pressure. Mycological and bacteriological studies ot the skin of the surface of the lesions revealed only normal observations. Biopsy was suggested, but, because of the obvious location of the lesions, we did not insist on that procedure when it was refused by the patient.

SUMMARY

A case of idiopathic atrophy of the skin of the face is reported. The history, course and varioliform and linear scars are suggestive of Heidingsfeld's atrophia maculosa varioliformis cutis.

Dr. Marion B. Sulzberger, Dr. Charles R. Rein and Dr. Max Jessner gave suggestions toward the preparation of this paper. Photographs were taken by Miss Eleanor Moreland.

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DYSTROPHIA UNGUIUM MEDIANA CANALIFORMIS

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Dystrophia unguium mediana canaliformis is a very rare and rather bizarre change affecting one or more nails, usually the thumb nails, in which a central, longitudinal, dark-colored streak appears for no apparent reason. Robinson and Weidman [1] reported a case in 1948 and listed

Fig. 1.—A photograph of the two thumb nails, showing the symmetry of the lesions, taken two months after the appearance of the defect.

the few previously reported cases back to the original one described in 1928 by Heller,[2] who named the condition.

The following case seems worth recording because of its curious periodicity and the exact symmetry of the lesions in the two thumbs.

REPORT OF A CASE

The patient was a fit, slightly built man of 33. He presented himself complaining of an abnormality of both thumb nails, illustrated in figure 1. About seven weeks before I saw him

1. Robinson, M. M., and Weidman, F. D.: Dystrophia Unguium Mediana Canaliformis, Arch. Dermat. & Syph. **57**:328 (March) 1948.

2. Heller, J.: Zur Kasuistik seltener Nagel Krankheiten. Dystrophia Unguium Mediana Canaliformis, Dermat. Ztschr. **51**:416 (Jan.) 1928.

he had noticed a defect at the base of each thumb nail. There was no discomfort and no apparent inflammation of the perionychial tissues. As the nails grew the deformities assumed a linear shape with a central fissure and radiating, dark-colored side branches sloping backward toward the base so as to give an arrowhead effect. There was perfect symmetry of the lesions.

This was the patient's fifth or sixth attack. The first had occurred when he was about 14 years old and the others at irregular but widely separated times since. His last previous attack had been in 1942. On each occasion his two thumbs were similarly affected but never any other nails. The linear deformity extended from the base until almost the whole length of the nail was affected. Then normal nail was again laid down, and as growth proceeded the lesion gradually disappeared as the nails were trimmed. At this stage the free edge of the nail plate was divided in two by the lesion. The total course of this odd change was about seven months.

There had never been any precipitating cause in the form of trauma, illness or local inflammation. Between attacks the nails were perfectly normal.

The patient did not know much about his relatives, but he was not aware of any other cases in his family. None of his three siblings was affected. He had never had any other skin trouble.

Fig. 2.—Drawings showing the evolution of the nail deformity. *A*, at about two months from onset. *B*, fully developed condition at about four months. *C*, regrowth of normal nail at about six months from onset.

He was seen again six weeks after the first interview. By this time the deformity had extended almost to the free border of the nails, but the proximal 2 to 3 mm. of each nail had grown normally, and so this episode had apparently ended.

COMMENT

As may be seen in the photograph the "canal" in this case was open along its length and was really a narrow slit in the nail. The lesion was rather more ragged than in other reported cases, but nonetheless there is little doubt that this was the same condition.

The most striking feature of this case was the complete normality of the perionychial tissues; even the cuticle was uninterrupted across the base of the nail. Robinson and Weidman were unable to obtain a detailed history of the evolution of the lesion in their case but thought it probable that it began as a split at the free edge. This seems unlikely in view of the repeated behavior of the condition in my patient.

Another curious feature was the periodicity of the disorder, which has not been previously reported. It seems quite certain that the central defect in the nails is the result of a failure of normal keratinization, and Robinson and Weidman demonstrate the appearance of parakeratosis in the nail adjacent to the central canal in their case. Why the particular cells in the matrix should misbehave in this manner, why they should do so only for a period of a few months once in every few years and why at the same time and in the same place in each thumb remains a complete mystery.

GENITOCRURAL PRURITUS FROM ORAL AUREOMYCIN

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Aureomycin is one of the newer and more important antibiotics used at present. Gastrointestinal symptoms and genitocrural burning and itching are among its severer side effects. These genitocrural symptoms may occur with or without diarrhea. We have recently observed and are reporting 13 cases of genitocrural pruritus from the oral administration of aureomycin. Erythema, edema, scratch marks and, in one case, secondary infection were noticed in the involved areas.

In treating these persons gratifying results were obtained from the use of an antihistamine ointment. Our experience was limited to the use of one particular ointment, but possibly the application of similar antihistamine ointments would give as good results. Patients reported pronounced relief and comfort within 24 to 36 hours after the local medication was first applied. One patient experienced relief within a few hours. In no case did symptoms persist longer than two to three days.

CASE HISTORIES

Four of the thirteen case histories are being reported.

CASE 1.—W. B. was a 79 year old white man with chronic cystitis of four years' duration. He also complained of extremely painful feet for which he had consulted many physicians and chiropodists. The cystitis was treated with aureomycin, 500 mg., given at six hour intervals. Anal itching occurred after six doses of aureomycin. An antihistamine ointment was then applied three times a day with complete relief in 24 hours. At the time of writing, the patient reported that he occasionally took aureomycin because it made his feet feel better. Each time the aureomycin was taken anal itching developed, but it had so far been relieved by the use of antihistamine ointment.

CASE 2.—H. B., a 26 year old white woman, was under treatment for atypical pneumonia which did not respond to penicillin or sulfadiazine therapy. She was then given 500 mg. of aureomycin every six hours for eight days. The pneumonic condition improved rapidly, but when the patient was seen eight days after her discharge from the hospital she complained of severe anal and vulvar burning and itching. Antihistamine ointment was applied, giving complete comfort. After four days it was no longer necessary for her to apply the ointment.

CASE 3.—F. D., a white woman aged 48, who had had a long-standing cardiac condition with some constant signs of passive congestion, acquired pneumonia of the lower lobe of the right lung. Aureomycin, 500 mg., was given every six hours. After the eighth dose the patient had mild diarrhea with intense anal and vulvar itching. An antihistamine ointment was used, with immediate relief of the itching and burning, and the patient continued to receive 500 mg. of aureomycin for eight more days.

CASE 4.—R. T., a 24 year old white woman, eight days post partum acquired pyelonephritis and mastitis. Aureomycin, 500 mg., was given every six hours. On the third day during the aureomycin therapy anal burning and itching occurred. The application of antihistamine ointment gave immediate relief, enabling the patient to continue aureomycin therapy without discomfort for three more days. It is interesting to note that the vulva and episiotomy wound were not involved.

Eight of the 13 patients had diarrhea in conjunction with the pruritus. The antihistamine ointment used locally for relief of the pruritus in these cases contained phenindamine (thephorin®).

COMMENT

Davis [1] and Harris [2] have reported among the side effects during the oral administration of aureomycin severe anal and perineal burning and itching. The local use of zinc oxide paste, hot

1. Hughes, J. D.: Treatment of Amebiasis with Aureomycin: Report of 38 Cases, J. A. M. A. **142**:1052-1054 (April 8) 1950.

2. Harris, H. J.: Aureomycin and Chloramphenicol in Brucellosis: With Special Reference to Side Effects, J. A. M. A. **142**:161-164 (Jan. 21) 1950.

applications and soothing ointments has not been too satisfactory in the control of these anal and perineal symptoms, and secondary infection due to scratching has in some instances produced pronounced discomfort. Parets [3] and Peck and Feldman [4] have shown that sensitization to aureomycin can and does occur. It is interesting to note that Shelmire [5] has reported that when allergic substances such as poison ivy oleoresin are given by mouth an anal and perianal pruritus can and often does result. He believed that the unabsorbed portion of the oleoresin probably came in contact with the perianal skin and caused the pruritus ani. In the cases in which pruritus develops during and after the oral use of aureomycin we feel that a similar situation occurs. The unabsorbed portion of the aureomycin which comes in contact with the anal, perianal and perineal skin acts as a sensitizer which in all probability causes the intense burning and itching.

We also know that aureomycin brings about a change in the intestinal flora. It appears to interfere with the various factors which limit Candida albicans growth. There is a definite increase in the amount of C. albicans, and this may in some cases be an added irritating factor.

An antihistamine ointment was used because we felt that the genitocrural burning and itching were probably due to the sensitizing and irritating effect of aureomycin on the anal, perianal and perineal skin. Phenindamine ointment was applied to the affected areas with pronounced relief of symptoms. The report of Strauss [6] as to the pronounced anesthetic and soothing effect of phenindamine used locally is of interest.

SUMMARY

We are reporting the occurrence of 13 cases of genitocrural burning and itching during and immediately after the oral use of aureomycin. We feel that these symptoms are probably due to the sensitization of the anal, perianal and perineal skin by the unabsorbed portions of the aureomycin. The increased growth and spread of monilia in the intestinal tract may be an added secondary irritating factor.

Antihistamine ointments are herein reported to be an effective method of controlling the genitocrural irritation. Phenindamine ointment was used in these cases, but in all probability other similar antihistamine ointments would be as satisfactory.

3. Parets, A. D.: Angioneurotic Edema and Rash Due to Aureomycin: Reaction in a Patient with Multiple Sensitivities, J. A. M. A. **143**:653-654 (June 17) 1950.

4. Peck, S. M., and Feldman, F. F.: Sensitivity Reactions to Aureomycin, J. A. M. A. **142**:1137-1139 (April 15) 1950.

5. Shelmire, B.: Hyposensitization to Poison Ivy, Arch. Dermat. & Syph. **44**:983-998 (Dec.) 1941.

6. Strauss, W. T.: Progress in Antihistamine Therapy, J. Am. Pharm. A. (Practical Pharmacy Ed.) **9**:728-737 (Dec.) 1948.

IMPETIGO HERPETIFORMIS TREATED WITH AUREOMYCIN

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A case of probable impetigo herpetiformis, of four weeks' duration, terminated under aureomycin therapy after eight days, is herewith reported because of its rarity and usual resistance to other means of therapy.

In 1872 Hebra [1] described five cases of an eruption occurring in pregnant and puerperal women, pustular from the first and grouped in a circinate manner. In 1883 Kaposi [2] reported 11 cases of impetigo herpetiformis (including Hebra's five) in women. All the patients ultimately

1. von Hebra, F.: Wien. med. Wchnschr. **22**:1197, 1872; Lancet **1**:399, 1872.

2. Cited by Duhring, L. A.: Am. J. M. Sc. **88**:391, 1884.

died without significant observations at autopsy. In 1887 Kaposi [3] reported the cases of two more patients (who died), one of whom was a man. Since then cases have been reported in men and women and in girls and boys.[4]

References [5] to Hebra's description stress the following features: (*a*) pustules from the first, (*b*) characteristic grouping in rings or portions of rings, (*c*) formation of new groups of pustules at the peripheries of the rings, (*d*) drying of pustules into flat yellow crusts, (*e*) absence of itching, (*f*) fever and constitutional symptoms, often with prostration, and (*g*) pronounced brownish pigmentation left on healing.

Ormsby mentions in his textbook [6] the tendency of the disease to begin in the groin and to involve the mouth and throat. In 1944 A. F. Hall [4] reported a case of successful treatment with sulfapyridine. In 1948 Teodorescou and Conu [7] reported on a patient treated with penicillin, and they have also reported on one treated with one of the sulfonamides. No previous patients have been treated with aureomycin, so far as I am aware.

REPORT OF A CASE

J. J. W., a 42 year old real estate agent of Anglo-Saxon descent, was in good health until April 7, 1950, at which time he noted a group of pustules on the vertex of his scalp at his bald spot. These did not itch at all but would crust and catch in his comb. He continued to feel well, apart from the annoyance of succeeding crops of pustules on his scalp, until April 20, at which time groups of pustules simultaneously appeared on his scrotum and penis and sores appeared in his mouth. He began to feel ill and, although he was very busy, consulted his family physician. His physician gave him brewer's yeast tablets by mouth, and crude liver injections twice weekly for three injections. New crops of pustules continued to appear in the groin, and his mouth and throat became very sore, so that chewing and swallowing food became difficult and painful. On May 1, his physician referred him to me.

On examination his temperature by mouth was found to be 100.2. The mouth and pharynx showed numbers of grayish puffy patches, well defined and about the size of a dime and slightly smaller, as well as ragged erosions about the same size, extending as far down the pharynx as could be visualized. The mucous membrane of the tongue, cheeks and palate was involved. The first impression was that these lesions were flaccid and ruptured bullae. The vertex of the scalp presented small crusted pustules suggesting acne necroticans miliaris, some of which had been excoriated by a comb. They were surrounded by a thin margin of purplish inflammatory erythema and were grouped in a circinate manner. The groin presented the most remarkable picture of all. Here there were large (1 cm. in diameter) pustules arranged in rings and whorls, with other rings extending off the edges of older rings, some pustules showing central umbilication, and some crusting. A purple inflammatory halo surrounding each pustule was a striking feature. There were no macular or vesicular lesions. The pus was thick and grayish and opaque and could only with difficulty be expressed. The glans penis, scrotum and thighs were profusely involved. These areas had recently been causing pain. The inguinal glands were not enlarged.

Examination of the rest of the patient's skin showed no additional lesions. Questioning of the patient concerning possible exposure to vaccination, herpes simplex, smallpox, etc., gave no lead to the possible causative factor. There had been no recent illness. The patient had had all the usual childhood diseases early in life.

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3. Kaposi, M.: Vrtljschr. f. Dermat., Wien, **14**:275, 1887; cited by Tenlen, S.: Acta dermat.-venereol. **18**:165, 1937.

4. Hall, A. F.: Impetigo Herpetiformis in Male: Report of 1 Case with Response to Sulfapyridine, Arch. Dermat. & Syph. **50**:107 (Aug.) 1944.

5. Heitzmann, C.: Arch. Dermat. **4**:37, 1878.

6. Ormsby, O. S., and Montgomery, H: Diseases of the Skin, ed. 6, New York, Lea & Febiger, 1943, p. 403.

7. Teodorescou, S., and Conu, A.: Ann. dermat. et syph. **8**:149, 1948. Frank, L. J.: Impetigo Herpetiformis: Report of Successful Treatment with Sulfanilamide, Arch. Dermat. & Syph. **40**:253 (Aug.) 1939.

With a mental reservation that the disorder might be a case of impetigo herpetiformis or an atypical case of Kaposi's varicelliform eruption or erythema multiforme and with a recommendation that the patient go straight home to bed, I placed the patient on the following treatment: administration of aureomycin capsules, 250 mg., one every four hours for four doses daily; application of bacitracin ointment (500 units per cubic centimeter) in repeated small doses three times daily to groin and scalp, and the sucking of aureomycin troches, one every two hours.

The next day the patient called to say he was very much better and that, since he had many things to do, he didn't think he would go to bed. At the end of four days the pustules had almost entirely cleared, leaving a brownish pigmentation at the sites. The patient was enjoying his meals and felt well and could only with difficulty be persuaded to continue taking his aureomycin doses, which he did for a further four days. At the end of this time there were no active lesions anywhere and healing was almost complete. The patient could not be convinced that he should continue taking aureomycin and did not return again to the office. On October 1 the family physician informed me that the patient had remained well and was carrying on his business vigorously as usual.

COMMENTS

Unfortunately, the patient refused to allow photographs to be taken or biopsies to be made, so that definite proof of the diagnosis cannot be offered. Discussion of the case subsequently and comparison of photographs of proved cases with other dermatologists led to the conclusion that the case was of unusual interest and should be reported in view of the often fatal prognosis of this peculiar entity.

The dramatic response to aureomycin therapy here would suggest that impetigo herpetiformis is an entity unrelated to herpes simplex, dermatitis herpetiformis, Kaposi's varicelliform eruption, pemphigus vegetans or erythema multiforme, in which aureomycin therapy has often been very disappointing. It is concluded that impetigo herpetiformis indeed truly exists as an entity, although it is of obscure etiology and fortunate rareness.

SUMMARY

A case of probable impetigo herpetiformis with dramatic recovery after aureomycin therapy is herewith reported.

CONTACT DERMATITIS CAUSED BY BAMBOO

BENCEL L. SCHIFF, M.D.*
PAWTUCKET, R. I.

Recently I was called to investigate an outbreak of dermatitis in a factory that manufactured tennis rackets made of bamboo. The bamboo used was in long strips, devoid of bark and hair, and prior to being molded into shape it was put through a sanding process. A check of dermatological literature revealed no reports of any dermatitis due to bamboo. It is felt, therefore, that the following cases are worthy of report.

REPORT OF CASES

Case 1.—R. M., aged 50, had been a bamboo sander for the past 30 years. He was first seen by me on April 1, 1950, and presented an erythematovesicular, oozing and crusted dermatitis involving the dorsal and palmar aspect of both hands, the volar and ulnar surfaces of both forearms and the neck and face, accompanied with severe itching, of two weeks' duration. He gave no history of previous skin disease. He related that recently a new shipment of bamboo had arrived from Japan and that when the process of sanding the new bamboo was started he had experienced itching of fingers, hands and forearms; a few days later the eruption had appeared, involving the locations mentioned above. The patient was told to stop working, and symptomatic topical treatment was ordered. There was great improvement after four

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days of treatment. The patient was given patch tests on April 10, 1950, with scrapings of the bamboo, and after 24 hours a positive reaction consisting of a vesiculobullous lesion was noted on the area tested. On April 19, 1950, the dermatitis had subsided, leaving pigmentation, and the patient returned to work with instructions to use protective covering. When seen two weeks later, he had no recurrence of the dermatitis.

CASE 2.—J. D., aged 22, was seen by me on the same date. He had been employed at the factory for only three weeks. He showed lesions similar to those in case 1, and on the same sites. Patch testing with bamboo scrapings elicited a 4+ reaction. On April 21, 1950, when the dermatitis was cleared, the patient returned to work, but in spite of protective covering at his work, the dermatitis recurred, and the patient was transferred to another type of work in the factory, not involving contact with bamboo.

CASE 3.—A. G., aged 51, was also seen by me on the same date. He had been employed for six weeks as a bamboo sander. He presented an exact duplication of the aforementioned dermatitis. Patch testing with bamboo scrapings elicited a 4+ reaction. On April 23, 1950, after the dermatitis had subsided, the patient returned to work. However, even after he had used all necessary protective coverings, the dermatitis recurred in severe form, and the patient was shifted to another department.

COMMENT

Three cases of contact dermatitis due to bamboo, with positive patch test reactions, are reported. The dermatitis involved the exposed parts and was very pruritic. On healing of the dermatitis, a deep brownish pigmentation was noted on all parts involved. It is believed that the reason the patient in case 1 had no recurrence on reexposure was, in all probability, "hardening," since he had worked for 30 years at this occupation.

251 Broadway.

Correspondence

FURTHER STUDIES ON THE MECHANISM OF ADHESIVE TAPE DERMATITIS

To the Editor:—In the paper by Peck, Michelfelder and Palitz which was published in the ARCHIVES under the title of "Further Studies on the Mechanism of Adhesive Tape Dermatitis" (**63**:289 [March] 1951) certain points raised by these observers call for comment. These points are mainly concerned with the question of allergic adhesive tape responses, their alleged rarity and the supposed difficulty in tracing their cause or causes. Concerning such instances, Peck and co-workers concluded, "This reaction is rare. It is practically impossible to trace the specific sensitizer in any adhesive because the chemical composition varies from batch to batch."

1. Allergic contact dermatitis due to adhesive tape is not a rare occurrence. It may be relatively uncommon in terms of the percentage of people using this product. In some cases the hypersensitiveness is known to the patient; in other instances, to the dismay of the physician, this response may be encountered incidentally in the course of patch testing. The further study of these patients will require other technics of testing. Considering the almost universal use of various adhesive tapes, it is fair to state that, whereas this type of reaction may be relatively uncommon in the aforementioned sense, it is certainly not rare in an absolute sense.

2. The attitude that it is practically impossible to trace the specific sensitizer because the chemical composition varies from batch to batch is entirely too pessimistic and may tend to discourage research in this direction. I have, for example, recorded five cases of allergic adhesive tape dermatitis, in which the etiologic agent or agents were found (glycerine abietate, dehydrogenated rosin, Beni Para rubber, pitch subcompound and so forth). [The experimental details were recorded in following articles: Keil, H., and Bereston, E. S.: Dermatitis Due to a Transparent Adhesive Tape, ARCH. DERMAT. & SYPH. **45**:1052 (June) 1942; Keil, H.: Hypersensitivity to Adhesive Tape: Report of Four Cases Showing Its Variable Etiology, *J. Indust. Hyg. & Toxicol.* **25**:238 (June) 1943.] It is true that adhesive tape may have a variable composition, but this variability occurs within definite limits that can be appreciated and the problem may be overcome with a little knowledge of the physicochemical principles involved and with a little cooperation on the part of the manufacturer. It is evident that in the cases of nonallergic adhesive tape reactions, no matter how severe they may be, patch testing will yield negative or insignificant results. As for the postulation of new chemical compounds or systems in the completed adhesive tape, there is as yet no compelling evidence that such phenomena occur, and, for the moment at least, I would list this opinion among those that would benefit from the application of Ockham's razor.

HARRY KEIL, M.D., New York.

Society Transactions

PHILADELPHIA DERMATOLOGICAL SOCIETY

Captain Robert L. Gilman (MC), USN, *Chairman*
H. E. Twining, M.D., *Secretary*
April 21, 1950

Urticaria Pigmentosa (Adult Type). Presented by DR. VAUGHN C. GARNER.

N. R., a white man aged 59 years, presents profuse, widespread, macular and maculopapular pigmentary lesions involving the scalp, face, trunk and the proximal segments of the extremities. The unusual clinical features are the late onset (at 56 years of age), profuse character of the eruption, extensive pigmentation, pronounced urtication on stroking, the almost axial distribution of part of the eruption and the poikiloderma-like changes in the groins.

A complete blood count and the blood sedimentation rate were within normal limits. Results of urinalysis were normal, and the serologic tests for syphilis gave negative reactions.

DISCUSSION

DR. VAUGHN C. GARNER: I emphasized on the protocol the late age of onset. I find that a series of cases discussed by Hannay in 1925 included approximately 280 patients. He found that only five of the group, less than 2 per cent, had acquired the eruption past the age of 50.

Mycosis Fungoides? Bowen's Disease? Presented by DR. VAUGHN C. GARNER.

T. E., a white woman aged 77 years, presents numerous widely scattered psoriasiform plaques with much annular and arciform configuration and with infiltrated edges. Other lesions are superficial and slightly scaly without infiltration. The face, hands and feet are free of the eruption. The patient's general health is good, except for colitis. She had typhoid in 1898 and a hysterectomy in 1919.

The medical examination revealed no abnormality except arteriosclerosis. The complete blood count was within normal limits. The serologic tests for syphilis gave negative reactions.

The report on the biopsy (Dec. 17, 1948) was as follows: "The epidermis was remarkably acanthotic. The pegs were irregular but still were elongated to a fairly uniform distance. Basal cells were uniformly of squamous type. From place to place certain cells contained large vacuoles and fused into small 'cysts.' The nuclei of such cells were pyknotic and otherwise degenerate. Moreover, numerous examples of dyskeratosis appeared, more particularly in the upper half of the epidermis. The writer found only one or two mitotic figures. A moderate infiltration of inflammatory round cells extended along the subpapillary plexus of vessels. Pathologic diagnosis: Paget's disease of the skin, later changed to Bowen's disease in consideration of clinical features" (Dr. Weidman).

DISCUSSION

DR. CHARLES R. REIN, New York (by invitation): Clinically, I thought the condition was mycosis fungoides, but another biopsy should be made.

DR. EDWARD F. CORSON: I thought that clinically it resembled mycosis fungoides.

DR. FRED D. WEIDMAN: I agree that when I first looked at the patient tonight I thought the disorder was mycosis fungoides, but there has never been any involvement above the neck; the lesions have never itched, and there is a very thin, tissue-paper-like atrophy in the center of the lesions which I thought did not conform to the picture for mycosis fungoides. A section from this case was sent to me, and it showed the features of Bowen's disease.

DR. JOSEPH V. KLAUDER: This is an extraordinary case. I would hold the diagnosis in abeyance pending further clinical observation and repeated histologic examination. I have never seen a case of Bowen's disease as widespread as the one this woman presents unless the patient had taken arsenic. I would not be willing to make a clinical diagnosis of mycosis fungoides; the disorder lacked the infiltration and features that would otherwise characterize mycosis fungoides. It had a peculiar configuration that suggested a late secondary syphilid, and the woman very pertinently said, pointing to one circinate lesion, "Everybody says this looks like something I don't have."

DR. VAUGHN C. GARNER: It has been interesting to watch the evolution of this condition. At the patient's first visit the patches were so superficial and scaly that one had to exclude the possibility of psoriasis, although I did make a clinical diagnosis of premycotic mycosis fungoides. Many of the lesions have changed materially in character. Some have become infiltrated, while others have assumed arciform and annular configurations. I was perturbed when I received Dr. Weidman's original report that this was Paget's disease, but I was willing to accept Bowen's disease as a compromise.

Leukemia Cutis? Presented by DR. H. E. TWINING.

W. F., a white man 50 years of age, presents numerous erythematous, rather sharply defined, slightly indurated macular and papular lesions confined to the back. Many have the appearance of wheals but are persistent. They vary from one to several centimeters in diameter. There is no evidence of vesiculation or ulceration. The liver and spleen are not palpable, and there is no evidence of enlarged lymph nodes. When the patient was examined in January 1950, he stated that in August 1949, while he was on vacation in New England, wheal-like lesions developed on his back. They were pruritic, and the condition was diagnosed as food poisoning (urticaria?). He was informed by an allergist after scratch testing that he was allergic to bananas, chicken, coffee and house dust. In 1945 a "full feeling," accompanied with vertigo, developed in the left ear.

The serologic tests for syphilis gave negative reactions. The results of a urinalysis and three complete blood counts were within normal limits. Aspirated bone marrow was essentially normal.

The report on the biopsy was as follows: "The epidermis could be normal for a position like the back. In the corium, pathologic changes were confined to the lymphatic spaces around the blood vessels, sweat ducts and pilosebaceous apparatus. All of the blood vessels were concerned, whether those of the superficial horizontal plexus or ones that are extending to midcorium, i. e. the perpendicular vessels. The perivascular mantles consisted of mature lymphocytes; they were narrow but densely packed with cells. A particularly large mass of cells lay in relation to a sebaceous gland at the bottom of the section, thus speaking for the depth of the processes" (Dr. Weidman).

DISCUSSION

DR. MAX JESNER, New York (by invitation): There are some rather well defined lesions on the back of the arm, consisting of purely lymphocytic infiltration. We have seen a number of such cases in recent years. I think they are similar to those described by Pinkus of granulomas localized on the face. The diagnosis is lupus erythematosus. Histologically, all these cases have a very massive, deep infiltration of round cells. These patients that have been followed have not manifested any pathologic blood picture. The lesions often clear in the center and are somewhat progressive, with remissions and exacerbations. We are trying to collect such cases in order to determine the etiology. I am unable to say where they should be classified, whether in the Spiegler-Fendt sarcoid group or with the lymphocytomas.

DR. CHARLES M. REIN, New York (by invitation): A striking feature is that the condition tends to subside almost completely without treatment. It resembles erythema multiforme. This man states that his lesions have disappeared considerably with the use of simple shake lotions.

A patient of mine has had the condition for three years. He has had several exacerbations, but the eruption disappears without any therapy.

DR. FRED D. WEIDMAN: I made the histologic diagnosis in this case. I admitted that the infiltration was not as deep at it should be for leukemia cutis but could not think of any other disorder in which the configuration was so monomorphous. I cannot think of any other condition just now in which that is the case. I am disappointed that we cannot make a diagnosis.

Tuberous Sclerosis with Obstruction of Aqueduct and Internal Hydrocephalus with Collagenous Plaques in a Five-Month-Old Boy. Presented by DR. H. E. TWINING and DR. CARROLL F. BURGOON JR.

The medical examination resulted in essentially normal findings except for neurologic findings of hyperactive reflexes, spasticity and congenital coloboma.

The report on the biopsy (March 31, 1950) was as follows: "Dense collagen hyperplasia of corium, otherwise nothing specific can be seen in section."

DISCUSSION

DR. THOMAS BUTTERWORTH, Reading: The collagenous plaques that occur in tuberous sclerosis usually occur on the back or the flanks. Seldom are they as numerous as in this patient. It is rather difficult to make a diagnosis of tuberous sclerosis for this child at the present time. Some years ago we segregated eight mental defectives with epilepsy and collagenous plaques and have seen adenoma sebaceum develop in one of them. In most cases adenoma sebaceum does not develop until the fourth or fifth year. There may be some mental retardation in this child later in life.

DR. H. H. PERLMAN: Does Dr. Butterworth think the lesions the counterpart of adenoma sebaceum? Is there any correlation between the two?

DR. THOMAS BUTTERWORTH, Reading: In about 75 or 80 per cent of our cases of adenoma sebaceum there will be collagenous plaques on the back or flanks. Time and again, when a case is shown there is discussion over whether the condition is multiple benign cystic epithelioma or adenoma sebaceum; however, if one examines the back the question is answered, because there are no collagenous plaques in multiple benign cystic epithelioma, but these lesions are present in tuberous sclerosis.

Urticaria Pigmentosa (Adult Type); Osteoarthritis. Presented by DR. CARROLL F. BURGOON JR. and DR. H. E. TWINING.

Dermatomyositis. Presented by DR. CARROLL F. BURGOON JR. and DR. H. E. TWINING.

Micronychia? Presented by DR. CARROLL F. BURGOON JR. and DR. H. E. TWINING.

Vogt-Koyanagi Syndrome. Presented by DR. THOMAS BUTTERWORTH.

Congenital Ectodermal Dysplasia. Presented by DR. HERMAN KLINE, Atlantic City, N. J.

Robert L. Gilman (MC), U.S.N., *Chairman*

H. E. Twining, M.D., *Secretary*

May 19, 1950

Sarcoid; Primary Optic Atrophy. Presented by DR. DONALD M. PILLSBURY and (by invitation) DR. W. T. FORD.

DISCUSSION

DR. COLIN CAMPBELL (by invitation): My associates and I have followed about 20 cases of sarcoid in the past months, treating them with urethan. This drug is used in multiple myeloma with good effects and in myelogenous leukemia with some improvement. The first patient in our series was one with sarcoidosis accompanied with an elevated temperature. Urethan was used with success; there was a rapid subsidence of fever, and the patient improved considerably. Twenty patients have been given the drug for periods varying almost up to a year in a dose

of 3 or 4 Gm. to tolerance, daily. We have had six patients with cutaneous lesions; four have shown improvement, and two have not. One patient who improved was given 30 Gm. intravenously over a period of 10 days. She had had her lesions intermittently for 15 years. We have found it difficult to evaluate this therapeutic agent, particularly when dealing with the cutaneous lesions of sarcoidosis.

The mechanism of the action of this drug is not completely understood. It has been shown to produce adrenal hypertrophy in laboratory animals, and it has been shown to be a mitotic poison. Toxicity is exhibited frequently, and for this reason patients must be seen at frequent intervals. Leukopenia is the most serious complication. It has been our practice to discontinue therapy when the white cell count has fallen to about 3,000 per cubic millimeter. After the drug has been withheld a few days, the white count has almost invariably returned to normal. Gastrointestinal symptoms (nausea, vomiting and anorexia) are extremely frequent. Hepatitis has been reported, and we have seen it in two cases. Whether it is a concomitant viral infection, is due to the drug or has an entirely different mechanism we do not know. With intravenous therapy, pulmonary edema occurs and must be watched for carefully. The pulmonary lesions in some of the cases have shown considerable improvement. In acute uveitis there have been fairly good results, but not with the chronic form. We have treated one case of sarcoidosis in the past two weeks with cortisone. The patient's cutaneous lesions regressed markedly, and his cough disappeared.

DR. CARROLL F. BURGOON: I think it was in 1945 that Sievers reported in the *Southern Medical Journal* on four patients with sarcoidosis treated with nitrogen mustard all of whom did well. The observation period, however, was very short.

DR. BERNARD L. KAHN: Along the line of Dr. Jones's initial discussion, we followed a patient for four or five months without observing any changes in her symptoms. We have had her on the prescribed dose, namely, 4 Gm., later decreased to 3 Gm. because of leukopenia. Her cutaneous symptoms have cleared about 60 per cent during treatment. There has been no change in the serum protein readings or pulmonary infiltration.

DR. CARMEN C. THOMAS: Through the courtesy of Dr. Harold Israel and Dr. M. Sones, I have had the opportunity of seeing a patient with sarcoidosis treated with cortisone, whose cutaneous and mucosal lesions and lymph node and pulmonary involvement had remained practically stationary for three years. On administration of 200 mg. of cortisone daily over a period of seven days the lesions melted away. Histologically, it was most striking to see the changes which occurred—the disappearance of organized tubercles and the substitution of a disorganized mass of cell tissue with complete disappearance of lesions from the mucosal surface in three or four days and from the skin within a week. Unfortunately, the patient had undesirable by-effects—epileptiform seizures and a psychosis from which she is still suffering.

DR. COLIN CAMPBELL (by invitation): In analyzing our data we have used signs of improvement in the serum protein readings as the main objective; if one follows the changes in the albumin-globulin ratio and the serum globulin fractions, one will find maximum improvement to occur somewhere between three and four months after the beginning of therapy. We wonder whether it is impracticable to continue therapy longer than that time. We have not seen anyone have an appreciable improvement after four months.

Anthropoid Primate Ringworm: A Type of Microsporum Audouini Infection in Monkey and Owner. Presented by DR. JOHN P. SCULLY and (by invitation) DR. ALBERT M. KLIGMAN.

The owner acquired ringworm of the glabrous skin and noted subsequently that the monkey's hair was falling. Culture from both owner and monkey yielded M. audouini. The monkey's hair is Wood light positive. The strain of M. audouini is exceptional in that numerous macroconidia are produced. The monkey has received no treatment but will be carefully observed during and especially after puberty.

DISCUSSION

DR. FRED D. WEIDMAN: I have seen other monkeys with this kind of mycotic disease of the skin but have never isolated M. audouini; the organism has been Trichophyton gypseum.

The culture tonight appeared perfectly typical for M. audouini. However, it grew very rapidly and there were many fuseaux, so that there is more work to be done before the diagnosis of M. audouini infection is definitely established.

DR. ALBERT M. KLIGMAN (by invitation): The organism is Microsporon audouini, without a doubt; however, it has a peculiar nutritional characteristic. As you know, it is anthropophilic and does not ordinarily attack lower animals, because they are immune to experimental infection. The "human" nature of the host in this disease is emphasized by the fact that when the animal was taken into the darkroom and examined under the Wood light, it manifested symptoms of conversion hysteria and fell to the floor in a dead faint. We inoculated the fungus into a few volunteers and have no doubt that the infection can be transmitted rather readily. It is not difficult to implant M. audouini on the glabrous skin of the human being.

Sclerosing Hemangioma Type of Nevoxanthoendothelioma in a Five Month Old Child. Presented by DR. MEYER L. NIEDELMAN and DR. ADOLPH BLEIER.

DISCUSSION

DR. HERMAN BEERMAN: I doubt the propriety of the diagnosis of sclerosing hemangioma in this case. I would call this condition an example of nevoxanthoendothelioma. I should also like to point out that nevoxanthoendothelioma, especially if it has any visceral manifestations, as in the case of Blank, Eglick and Beerman (*Pediatrics* **4**:349 [Sept.] 1949), is probably a form of Hand-Schüller-Christian disease.

DR. MEYER L. NIEDELMAN: There is one theory, expressed by Lever in his text on histopathology, that nevoxanthoendothelioma, histiocytoma and sclerosing angioma are variants of the same process, the exact diagnosis depending on the clinical and histologic observations. Nevoxanthoendothelioma probably represents the early or young lesions of histiocytoma, and when the histioctyes attempt to form new blood vessels and become engulfed by fibroblasts, the disorder is called sclerosing hemangioma. The histiocyte is the parent cell of the fibroblast and may develop into a fibroblast. The development of collagen in these tumors would suggest a progressive state. As no foam cells or foreign body giant cells were found in this case and there were numerous vascular spaces lined by endothelial cells and very few histiocytes, the picture would suggest a diagnosis as presented.

Xanthoma Tuberosum Multiplex. Presented by DR. BERTRAM SHAFFER and (by invitation) DR. WILLIAM W. WELLS.

Xanthoma Tuberosum Multiplex: Treatment with Fat-Free Diet. Presented by DR. BERTRAM SHAFFER and (by invitation) DR. WILLIAM W. WELLS.

DISCUSSION OF PRECEDING TWO CASES

DR. FREDERICK URBACH (by invitation): This afternoon I was talking to some of the staff men in the department of gastroenterology who have been able to develop a diet completely free from fat, both animal and vegetable. They have followed two patients with cardiovascular disease, one of whom has xanthoma tuberosum and one, a lesion of xanthelasma. Both had cholesterol values of around 600 mg. per 100 cc. On the fat-free diet mentioned the blood cholesterol was brought down to 150 or 160 mg. per 100 cc. These staff men referred to have checked on normal persons and are convinced that the blood cholesterol level can be lowered by putting patients on a diet containing 15 Gm. or less of total fat, irrespective of the initial level. In spite of Dr. Thannhauser's statement that a low fat diet has little effect on the lesions of xanthoma, I think that this investigation suggests otherwise.

DR. FRED D. WEIDMAN: The late Dr. Urbach treated two of his patients which I saw on a low fat diet. He reduced the vegetable as well as the animal fats, and there was no question regarding the extreme regression of the lesions under that regimen.

DR. CARROLL F. BURGOON: Gofman of the University of California at Berkeley, writing in *Science*, showed that there were different lipoproteins and that, although the total values may be normal, there are variations in the fractions.

DR. FREDERICK URBACH (by invitation): In the experimental studies undertaken here it was demonstrated that the addition of 50 Gm. of vegetable fat to the previously fat-free diet caused a rise in serum cholesterol. It would thus appear that the reduction of vegetable fat intake is as important as the exclusion of animal fat and cholesterol.

DR. BERTRAM SHAFFER: Clinically the cases are xanthoma tuberosum. These are classified as the hypercholesterolemic type of xanthomatosis by Thannhauser. The absence of hypercholesterolemia does not negate the clinical diagnosis, as this case illustrates.

Papulonecrotic Tuberculid. Presented by DR. JOHN P. SCULLY, Reading.

K. F., a white woman aged 31 years, presents (1) tiny, depressed scars, (2) brownish, scaling or crusted papules of right external pinna and adjacent scalp area and (3) a few grouped, similar lesions on the left cheek and the tip of the nose. They have been present for upward of two years. The family history and the patient's past history are noncontributory.

A systemic review revealed no abnormality. The Vollmer patch test reaction was negative. The serologic tests for syphilis gave negative reactions.

The report on the biopsy specimen was as follows: "There was a deep erosion at one end of the section, covered by a thick layer of crust. Immediately below the necrotic parts a poorly demarcated zone of tuberculoid tissue appeared; in it there was a diffuse arrangement of epithelioid cells, a few lymphocytes and a bare suggestion of multinucleation in some of the cells without being quite the genuine giant cell. It required very careful study to recognize that there were some places where the epithelioid cells were focalized, that is, were not intermixed with lymphocytes. In no case was there any formation of definite miliary granulomas such as are surrounded by a definitive zone of lymphocytes.

"The above changes extended only a short distance below the surface. The deeper parts of the corium were thickly studded by nicely rounded aggregations of densely packed lymphocytes, and a blood vessel could usually be defined somewhere within them. That is, there was a dense perivascular lymphocytic infiltration.

"In the absence of any indications of syphilis, I have to decide in favor of tuberculosis. In view of the very high grade of lymphocytic reaction, this patient should have a very high rate of allergy, and the intradermal tuberculin test should be very strongly positive. With the addition to this observation of the fact that the processes at the erosion were largely necrotizing, the circumstances seem to add up to a diagnosis of papulonecrotic tuberculid." (Fred D. Weidman).

DISCUSSION

DR. A. STRAUSS: I feel that this is a rather unusual case of papulonecrotic tuberculid, with lesions only on the ear.

DR. JOHN P. SCULLY, Reading: The patient has a few scars on the nose. I should like to call attention to the fact that reactions to the Vollmer patch test and first strength purified protein derivative tuberculin test were negaive. This observation is contrary to my conception of papulonecrotic tuberculid. When the patient came to the office there was some crusting on the back of the ear resembling seborrheic dermatitis. I prescribed the application of aureomycin locally, and the crusting disappeared after that therapy. Could this disorder possibly be a lupoid sycosis?

DR. BERTRAM SHAFFER: I have had two cases diagnosed clinically and histologically as papulonecrotic tuberculid, and in both the tuberculin test was negative. I cannot help feeling that in this country we see papulonecrotic tuberculid caused by other things—perhaps by the Staphylococcus.

DR. CARMEN C. THOMAS: I should like to confirm Dr. Shaffer's statement. I had a man under my observation for about two years who off and on had lesions indistinguishable from

papulonecrotic tuberculid which, after an infection of the finger, completely subsided under penicillin therapy. It was discovered that the patient had several devitalized teeth. When the teeth were extracted, he recovered completely, with no recurrence.

DR. H. H. PERLMAN: Isn't the asymmetry atypical of papulonecrotic tuberculid?

DR. FRED D. WEIDMAN: Clinically tonight I do not think the condition looks like papulonecrotic tuberculid, but I recall the section distinctly, and there is necrosis in that section. Moreover, it is a deep necrosis, and there are epithelioid cells at the base of the necrotic material. I do not see why, with regard to the question of symmetry, there should not be micro-organisms of low grade, indolent type other than the tubercle bacillus which produce the same type of reaction—the glanders organism, for example, and the virus of lymphogranuloma venereum. So we need not necessarily diagnose tuberculosis in this particular case. Nonetheless, one papule was necrotic, and that was the one I studied under the microscope.

Xanthoma (Tuberosum?) in a Boy Aged Six Years. Presented by DR. JOHN P. SCULLY, Reading.

Grouped Follicular Id (Bacterial, Fungus, Drug); Lichen Scrofulosus. Presented by DR. DONALD M. PILLSBURY and (by invitation) DR. MERLE HAANES.

Lupus Vulgaris. Presented by DR. HERMAN BEERMAN and (by invitation) DR. FREDERICK URBACH.

Calcinosis (Dystrophic) Cutis Circumscripta. Presented by DR. D. M. SIDLICK.

Urticaria Pigmentosa. Presented by DR. DONALD M. PILLSBURY and (by invitation) DR. MERLE HAANES.

Recurrent Bullous Eruption Analogous to Herpes Simplex. Presented by DR. D. M. SIDLICK.

Discoid Lupus Erythematosus(?); Sarcoid. Presented by DR. DONALD M. PILLSBURY and (by invitation) DR. MERLE HAANES.

Spiegler-Fendt Sarcoid / Drug Eruption? Presented by DR. H. E. TWINING.

METROPOLITAN DERMATOLOGICAL SOCIETY OF LOS ANGELES

David N. Alcon, M.D., *President*
Harold C. Fishman, M.D., *Secretary*
April 25, 1950

Parapsoriasis (Pityriasis Lichenoides Chronica, Juliusberg). Presented by DR. MAX POPPER.

DISCUSSION

DR. ELIOT WOLK: I noted that the nails were pretty well pitted, that point suggesting psoriasis. I should like to ask the presenter about that observation and its relationship to the diagnosis.

DR. MAX POPPER: I have observed the patient only a few weeks. This type of parapsoriasis resembles psoriasis. However, the following differential diagnostic distinctions can be made:

In psoriasis the scales are silvery white while in pityriasis lichenoides chronica they are yellowish white. Accordingly, in psoriasis the hyperkeratosis is pronounced while in pityriasis lichenoides chronica it is only moderate.

The scales in psoriasis can frequently be lifted as a thin film, while in pityriasis lichenoides chronica the scales are flaky. Accordingly, in psoriasis we find a uniform parakeratotic layer which tends to maintain the cohesion among the keratotic cells while in pityriasis lichenoides chronica parakeratosis is spotty only.

While the granular layer is missing in psoriasis we find the granular layer present in pityriasis lichenoides chronica. It is irregular in thickness, in spots forming "mole hills" of edematous granular cells.

The color of the psoriasis lesions is bright red or salmon; in pityriasis lichenoides chronica the color is yellowish red. Accordingly, in psoriasis we find tortuous papillary vessels, visualized through a few thinned rows of suprapapillary epidermis. In pityriasis lichenoides chronica the papillae are mostly obliterated and there is a tendency of flattened epidermodermis junction. Dilatation of vessels in pityriasis lichenoides chronica is missing or very slight.

While in psoriasis the lesions have a tendency to coalesce and to form plaques, in pityriasis lichenoides chronica lesions have the tendency to remain distinct.

In psoriasis there is an elevation and an infiltration of the lesions present; in pityriasis lichenoides chronica lesions are more macular.

In psoriasis the color of the lesions does not change on rubbing while in pityriasis lichenoides chronica the red color increases on rubbing.

A Case for Diagnosis: Persistent Severe Edema of Upper and Lower Eyelids Bilaterally with Proptosis and Ophthalmoplegia. Presented by DR. WILLARD L. MARMELSZADT.

F. R., a 46 year old man, five weeks ago felt a slight "soreness" behind his eyes. Within 24 hours his eyelids commenced to swell and reached their present size. Within several days he manifested a thin white discharge from the eyes which is worse in the mornings. His family physician treated him with antihistamine tablets for several days with no apparent effect. The patient consulted an ophthalmologist when injection of the conjunctivas and chemosis occurred. Eyedrops, which did not help or make worse his condition, were prescribed. Visual fields were measured and were normal. The patient then consulted a third physician, who gave a series of penicillin injections one week ago. This had no effect on the condition.

The patient is an apprehensive middle-aged man whose face presents a striking appearance. Both upper lids and, to a lesser extent, both lower lids show a tense shiny erythematous skin overlying areas of fairly firm edema. There is narrowing of the palpebral fissures and injection and chemosis of both the bulbar and the lid conjunctivas. Pupils are round and equal and react to light and in accommodation. Funduscopic examination revealed no abnormality. Ophthalmoplegia is present, especially noted when the eyes are rotated upward and outward. Definite proptosis is seen bilaterally.

Blood pressure is 160/120. There is moderate scaling on the scalp, and on the anterior portion of the chest wall, the glans penis and the left leg small patches of psoriasis are present. Thick scaling is present bilaterally on the soles of the feet. There are several classical splinter hemorrhages present under the finger nails of the left hand.

Laboratory data are as follows: Complete blood count—83 per cent hemoglobin, 10,500 white blood cells and 4,690,000 red blood cells; differential count—34 lymphocytes, 3 monocytes and 63 polymorphonuclear cells; urine—specific gravity of 1.010, negative reactions for acetone, sugar and albumin and occasional epithelial cells.

Treatment by previous physicians consisted in the administration of antihistamine drugs orally and penicillin injections.

DISCUSSION

DR. FRED F. FELDMAN: Since the presenter himself saw this patient for the first time today, he obviously could not make the studies which he would have liked to include with this presentation. In view of this, my remarks will be largely on theoretical grounds. Among other things, I should like to see basal metabolic rate, cholesterol and blood iodine studies done.

In addition to the edema of the eyelids and the proptosis this patient presents, there is swelling of the lower portions of the legs with superimposed early translucent papules. The latter observation suggests to me an early pretibial myxedema. I should like to see a biopsy performed to rule in or out such a possibility. The syndrome of exophthalmos plus pretibial myxedema following thyroidectomy is well known to all of us. At the April meeting of the Los Angeles Dermatological Society, Dr. Ben Newman and I presented a patient who had malignant exophthalmos plus pretibial myxedema following the use of radioactive iodine for the treatment of hyperthyroidism. Our patient, incidentally, showed pronounced improvement following cortisone therapy.

The patient tonight has many signs and symptoms suggesting a disturbance of thyroid metabolism. It is conceivable that he may fall into that rare group composed of patients with a thyrotoxic gland in whom the combination of progressive exophthalmos and/or pretibial myxedema may result without a thyroidectomy's having been done or thiouracil or radioactive

iodine's having been administered. In patients of this type it is postulated that sufficient thyroxin is not elaborated by the thyroid gland to inhibit the thyroid-stimulating hormone of the anterior lobe of the pituitary gland.

DR. WILLARD L. MARMELSZADT: One must consider a differential diagnosis of lid edema in this case. I thought when the patient first came in that he might have a severe angioneurotic edema. When I heard his story that the condition had been present six weeks and noted that it was so decidedly bilateral I thought I would look further.

Scleroderma Without Sclerodactylia? Lichen Sclerosus et Atrophicus (Multiple Areas of Morphea)? Presented by DR. ROSE B. SAPERSTEIN.

Rosacea-Like Tuberculid of Lewandowsky. Presented by DR. HAROLD C. FISHMAN.

Rosacea-Like Tuberculid of Lewandowsky. Presented by DR. EDWARD L. MURPHY.

Leukoplakia. Presented by DR. ROSE B. SAPERSTEIN.

Dermatitis Medicamentosa (Acetylsalicylic Acid). Presented by DR. EDWARD L. MURPHY.

Lupus Erythematosus. Presented by DR. IRVING A. LEWE.

Chronic Discoid Lupus Erythematosus: Case Presented for Suggestions for Therapy. Presented by DR. E. M. FAINER.

Lichen Planus? Post-Traumatic Vascular Defect? Presented by DR. ROSE B. SAPERSTEIN.

Pemphigus Foliaceus. Presented by DR. H. MORGAN, DR. M. BERKE and DR. A. W. GRAVES (by invitation).

Deferred Nevus (Tardus) Linearis. Presented by DR. ROSE B. SAPERSTEIN.

"Neurodermatitis" Due to Food Allergy (Egg). Presented by DR. STANTON B. MAY.

CENTRAL STATES DERMATOLOGICAL ASSOCIATION

H. N. Cole, M.D., Presiding

Annual Meeting, May 6, 1950

Facial Granuloma with Eosinophilia. Presented by DR. H. N. COLE, DR. J. R. DRIVER and DR. H. N. COLE JR., CLEVELAND.

H. A., a white man aged 54, has noted an asymptomatic lesion on the left cheek for the past three and one-half years, which has been slowly progressing in size. He denies any previous skin disease, or taking any medication internally.

Physical examination revealed an essentially normal condition except for a well circumscribed, slightly raised, moderately firm lesion on the left cheek, 6 by 8 cm. in diameter. The surface of the lesion was dry, smooth and slightly erythematous.

The reaction to the Kline test was negative. Results of examination of the urine were normal. The hemogram revealed 16.5 Gm. of hemoglobin and 5,200 white blood cells, with 67 polymorphonuclear leukocytes, 27 lymphocytes, 2 monocytes and 4 eosinophils. A test with old tuberculin in a dilution of 1:10,000 gave a negative reaction. The amount of serum protein and the albumin-globulin ratios were normal; the amounts of serum calcium and phosphorus were also within normal limits.

Histologic examination of a biopsy specimen showed an epidermis of usual and uniform thickness. The granular layer was distinct and one to three cells in thickness. The prickle cells were not remarkable. The basal cells were of uniform appearance and sharply demarcated from the corium, and no edema of these cells was observed. Several eosinophilic leukocytes were present in the epidermis. The upper part of the corium displayed a moderately scattered infiltrate, composed of neutrophilic and eosinophilic leukocytes, lymphocytes, occasional plasma cells and a considerable number of large, pale, mononuclear cells. In the deeper portion of the corium the infiltration was light and tended to be widely scattered. These changes were considered compatible with a diagnosis of granuloma with eosinophilia.

DISCUSSION

DR. HERMANN PINKUS, Monroe, Mich.: I agree with the diagnosis, that this case represents a type of granulomatous lesion of the skin cases of which have been published lately under the name of eosinophilic granuloma and which I should like to call facial granuloma with eosinophilia because in all the cases published so far, by now 10 or 12, the lesions have been on the face and only one of the patients also had lesions on other parts of the body. The present case has apparently been influenced by treatment. The patient says he had solid carbon dioxide applied

to this lesion, and I suppose that treatment accounts for some change in the clinical appearance, some of the scarring and pinkness in between the areas of purplish brown discoloration.

The histologic picture appeared typical, inasmuch as there was no change in the epidermis. There was a free zone just beneath the epidermis and then some granulomatous infiltrate in the middle part of the corium, which centered mainly around blood vessels. There did not seem to be many eosinophils, but there were many polymorphonuclear cells, mostly neutrophils, and in addition there were histiocytes, plasmacytes and lymphocytes. So, the histologic picture seems to bear out again that the term eosinophilic is not very well chosen in connection with these lesions. Some of them show many eosinophils, and others, like this one, have only a few, or even none.

As to therapy, apparently what has been done for this man seems to have had about as much effect as any therapy that has been recommended so far. The only other therapy seems to be complete excision, which of course would be impossible in this case. In some cases, like the case that Dr. Corbin and I have written up, the lesion has recurred even after excision. It would be very interesting to know whether destruction with carbon dioxide might be practical treatment for these lesions.

Pothmund's Syndrome. Presented by DR. H. N. COLE, DR. J. R. DRIVER and DR. H. N. COLE JR., Cleveland.

This case was discussed in a paper, "Congenital Cataracts in Sisters with Congenital Ectodermal Dysplasia (Rothmund's Syndrome)," published in *The Journal of the American Medical Association* (**129**:723-728 [Nov. 10] 1945).

DISCUSSION

DR. A. C. CURTIS, Ann Arbor, Mich.: The thing that impressed me was the peculiar scarring, many of the scars being linear and on areas which are easily traumatized, such as the knees, ankles and knuckles. It was my impression that both patients have cutis hyperelastica. The older child has very flexible fingers; you can take the index finger and almost superimpose it on the dorsum of the hand. That condition would explain the peculiar scarring in the absence of any bullous eruption.

A Case for Diagnosis. Presented by DR. GEORGE H. CURTIS, Cleveland.

V. J. D., a white housewife aged 30, states that she first noted a few red papules on the fingers of the right hand 12 years ago, while employed as a cook in a private home. For several months there appeared to be an increase in the number of lesions, but since that time the process has remained relatively stationary. There have been no subjective symptoms.

On physical examination there is observed to be slight exophthalmos and a somewhat diffuse enlargement of the thyroid gland, but other signs of hyperthyroidism are absent. There are about 50 discrete, round to oval, red to bluish red papules on the dorsa and sides of the fingers of the right hand. The surfaces of some are flat and waxy, and a scale may be scraped off with difficulty. There are no Wickham's striae.

The hemogram and urinalysis gave normal results. Bence Jones protein was absent. A sternal puncture was not diagnostic. The basal metabolic rate was —8 per cent. The blood Wassermann and Kahn reactions were negative. Roentgenograms of all bones and of the chest showed no pathological changes. Quantitative Mantoux tests with old tuberculin in dilution from 1:1,000,000 to 1:1,000 elicited negative reactions. The test with a 1:100 dilution gave a weakly positive reaction.

Histologic examination of a biopsy specimen prior to treatment showed atrophy of the epidermis. The basal cell layer was edematous and irregular. A large collection of cells, which included lymphocytes, fibroblasts, reticulum cells, plasma cells and mast cells in mixed proportion, was seen just beneath the epidermis.

Treatment has consisted in a course of 10 X-ray treatments, each being of 75 r, unfiltered. In addition, the patient also received a total of 10 weekly injections of bismuth subsalicylate. The papules became somewhat less pronounced, but after three months they had returned to the

pretreatment status. Treatment with oxophenarsine hydrochloride (mapharsen®) also failed to effect a change in the lesions. No treatment has been administered since August 1948.

DISCUSSION

DR. LEON GOLDMAN, Cincinnati: The first concern in this case was with the clinical differential diagnosis of the isolated papular, persistent type of lesions on the hand, with the curious, somewhat linear distribution. The clinical appearance, of course, suggested lichen planus or perhaps a form of flat wart. However, confusion arose on observation of the microscopic section. The characteristics of the reaction itself were quite puzzling because it had features ranging from those of lymphoblastoma or sarcoid all the way to those of lymphocytoma which seemed to be shown in one section. This type of distribution has never been reported in lichen planus. Also, I feel that this disorder is not a typical lymphocytoma because of its relative resistance to radiation therapy. In all probability it is some unclassified form of lymphoblastoma. I should like to see a biopsy of the changed papule at the present time.

Congenital Ichthyosiform Erythroderma. Presented by DR. IRVING L. SCHONBERG, Cleveland.

S. W., a white baby boy aged 22 months, presents a scaly eruption which first appeared when he was 4 weeks of age. This first developed over the scalp and gradually extended over the sides of the face and behind the ears, eventually involving the trunk and the extremities. Since birth there has been a laryngeal stridor, which is both inspiratory and expiratory. There has been impairment of hearing and wandering movement of the eyes.

Physical examination reveals a small, fairly well developed child, who presents over the scalp, face, ears, posterior portion of the trunk and extensor aspect of the extremities a fine, scaly, erythematous eruption. There is considerable crusting on the scalp and behind the ears. Examination of the eyes reveals that there is very little attempt to follow light. There is a wandering type of nystagmus. Macular areas of the eyes are normal. Examination of the ears, nose and throat reveals no abnormality. Direct laryngoscopy reveals a paresis of the right vocal cord and obstruction due to a large epiglottis. Rhonchi are heard throughout the chest. The heart appears normal. The liver edge is felt 3 fingerbreadths below the right costal margin. The spleen is at the left costal margin.

Urinalysis showed 1 to 2 white blood cells per high power field. Blood count revealed hemoglobin of 65 per cent, 3,540,000 red blood cells, 17,700 white blood cells and a differential count of 65 polymorphonuclear leukocytes, 32 lymphocytes and 3 monocytes. Blood chemistry determinations gave the following results: 290 mg. of total lipids, 102 mg. of cholesterol, 46.4 mg. of cholesterol esters and 230 mg. of lecithin per 100 cc. A cephalin flocculation test resulted in a 2+ reaction. The reaction to tuberculin was negative in a 1:1,000 dilution. A blood serologic test likewise gave a negative reaction. Roentgenograms of the chest showed diffuse infiltration in the medial portion of the lung fields. Roentgenograms of the long bones showed thickening of the periosteum of the femurs, tibias and humeri.

Histologic examination of a biopsy specimen showed hyperkeratosis, parakeratosis and acanthosis. There appeared to be an increase in the number of small vessels in the upper part of the dermis and a moderate amount of round cell infiltration about blood vessels and hair follicles.

Congenital Ichthyosiform Erythroderma. Presented by DR. NORMAN ASEL, DR. PAUL CHIVINGTON and DR. WILLIAM SPILLER for DR. JOHN E. RAUSCHKOLB, Cleveland.

P. V., a white girl aged 6 years, presents a skin abnormality which has been present since birth. The course of the disease has been characterized by the frequent occurrence of bullae, accompanied with redness and scaling.

The flexor and extensor surfaces of the extremities are about equally affected with an erythematous, scaling dermatitis, which has an ichthyosiform appearance in certain areas. Almost the entire body except the face is affected. Present on the sides of the neck, extremities and back are numerous bullae, which measure from 1.5 to 2 cm. in diameter.

Urinalysis and a complete blood count showed an essentially normal condition. The blood serologic reaction was negative.

Microscopic examination of a biopsy specimen showed pronounced hyperkeratosis and focal parakeratosis. The stratum granulosum consisted of one layer of cells. The stratum spinosum showed foci where the cells were vacuolated and dyskeratotic. The basal layer was intact. The upper portion of the cutis showed foci of lymphocytes, plasma cells and macrophages, located mostly about the blood vessels.

Bullous Congenital Ichthyosiform Erythroderma in a Girl Aged 17 Years. Presented by Dr. George H. Curtis, Cleveland.

L. R. D., a white school girl aged 17, gives the history of having had an erythematous bullous eruption since birth. Keratoderma of the palms and soles has been noted since early childhood. The family history is noncontributory.

Physical examination shows numerous dental caries. The skin is quite dry. In the sites of clothing constriction there is an increase in the number of flaccid blebs and bullae with erythematous bases. The skin in these sites is acanthotic and hyperpigmented. Bullae and grouped vesicles are sparsely distributed over the trunk and upper limbs. There is very little if any erythroderma. There is a moderate amount of lichenization and hyperkeratosis in the axillas, cubital fossae and inguinal region. Nikolsky's sign is not demonstrable. There are large plaques of dull red, thickened epidermis on the dorsa of the feet and ankles. Keratoderma of the palms and soles is prominent.

The hemogram, urogram, amount of fasting blood sugar and icterus index were all within normal limits. The Wassermann and Kahn reactions of the blood were negative. Plasma chlorides were 577 mg. per 100 cc. expressed as sodium chloride. Uroporphyrins were absent. A smear of blister fluid showed 6 eosinophils per 100 cells counted. The total serum protein was 8.5 Gm. per 100 cc.

Histologic examination of tissue from the posterior axillary fold showed a striking basket weave type of hyperkeratosis associated with hypertrophy of the epidermis. There were unusually large granules in the stratum granulosum Balloon cells of various sizes were present in the granular layer. The nuclei of about one half of the balloon cells were pyknotic. Sparse pigment granules were observed just beneath the epidermis.

Histologic examination of a herpetiform lesion showed a variation from large, dilated hydropic cells to a bullous lesion in the center of the section, separated from the dermis by a few strands of epidermal cells. The large bulla contained mostly polymorphonuclear leukocytes. The picture was one of so-called "colliquative vesiculation" with balloon cells. No inclusion bodies were seen in the sections stained with hematoxylin and eosin or by the Giemsa technic.

Because microscopic examination suggested a viral type of vesiculation, a rabbit's cornea was inoculated with material from an early vesicle, with negative results. Mild keratolytic ointments have been used. The administration of arsenic, vitamin D_2 and calcium, undecylenic acid, iron, sulfapyridine and multivitamin preparations has had no effect.

Congenital Ichthyosiform Erythroderma in a Man Aged 30. Presented by Dr. Norman Asel, Dr. Paul Chivington and Dr. William Spiller for Dr. John E. Rauschkolb, Cleveland.

A. S., a white man aged 30, gives a history of a generalized, erythematous, scaling disorder of the skin since birth. He has been presented before the Cleveland Dermatological Society on a number of previous occasions.

At this time he presents pronounced erythema, hyperkeratosis and scaling of the skin over the extremities. There is a vegetative type of hyperkeratosis on the dorsa of the toes, with some secondary infection. Pes equinus is noted. There is a shortening of the achilles tendons. The fingers of the hands are shortened and dystrophic, with thickening of the nails. The hair on the scalp is thinned, with diffuse redness of the scalp and face, accompanied with pronounced hyperkeratosis and scaling. The axillary hair is almost entirely absent.

Urinalysis and a complete blood count gave essentially normal results.

Histologic examination of a biopsy specimen showed many epithelial projections into the underlying stroma. Well developed intercellular bridges were present, and the basal layer was

regular in arrangement. There were some parakeratosis and hyperkeratosis. The granular layer appeared to be intact. A decided lymphocytic infiltration was observed in the upper part of the cutis.

DISCUSSION OF PRECEDING FOUR CASES

DR. LOREN W. SHAFFER, Detroit: This is an unusual group of four cases of a rare condition with various clinical manifestations. The diagnosis in the first case might be open to some question. The biopsy specimen presents mild ichthyosis. The picture in the groin, which is the main erythematous part, gave the impression of a possible superimposed Jacquet's dermatitis. Other unusual features are the mental condition present in the child, a spastic partial paralysis, the nystagmus and the eye symptoms, which are not part of the picture of ichthyosiform erythroderma. I think that this case will bear further observation.

The last case, of the dwarf with the verrucous, vegetative type of dermatitis, particularly on the legs, was an extremely interesting one. It was rather unusual that there was no involvement of the flexor areas of the body, which are usually involved in ichthyosiform erythroderma. The patient has pronounced hyperkeratosis of the skin along with the anomalies of growth and bone development. I thought that this case might have some relation to the case presented under the classification of hyperkeratosis congenita generalisata. Admittedly, in this case there was no cornubus, or cornified involvement, although there was some suggestion of that in the lesions of the legs.

Sturge-Weber Syndrome; Syringoma. Presented by DR. R. K. GARDNER, DR. J. J. STEWART and DR. J. G. THOMSEN for DR. H. N. COLE and DR. J. R. DRIVER, Cleveland.

S. J., a white man aged 22, has a widespread patchy red discoloration of the skin and mucous membranes which has been present since birth. At the age of 17 months, after a convulsive episode, a right spastic hemiplegia developed. Thereafter the patient's mental development was noticeably retarded. At the age of 19 his intelligence quotient was 53. For seven or eight years he has noticed numerous small, firm, painless, elevated lesions on the sides of the neck.

At the age of 2 months he was found to have a positive blood serologic reaction, as was his mother. A diagnosis of congenital syphilis was made, and he received eight intravenous injections of oxophenarsine hydrochloride (mapharsen®). The spinal fluid was found to be normal at the age of 17 months, the time of the convulsive episode. The patient has had progressively failing vision in the left eye since the age of 6 years and is now totally blind in that eye.

There is an extensive, patchy port wine stain involving the face, extremities and trunk, slightly more prominent on the right side. The buccal mucosa and pharynx are similarly involved. The head is asymmetric, the right side being more prominent while the right temple and the occipital protuberance are unusually prominent. There is a right spastic hemiplegia. On each side of the neck are numerous pale red papules, 3 to 5 mm. in diameter. The blood pressure is 165/115. A corneal opacity is present on the left, with only light perception remaining. Visual acuity of the right eye is nearly normal. There is slight constriction of the central visual field in the right eye.

The hemogram and results of urinalysis were within normal limits, except for a low specific gravity in urine concentration tests. The serologic test of the blood for syphilis gave a negative reaction.

Roentgenograms of the skull showed an extensive linear calcification in the left parieto-occipital region, interpreted as representing a chronic subdural hematoma with calcification. Roentgenograms of the kidneys revealed congenital polycystic disease.

Histologic examination of a papule from the left side of the neck showed changes consistent with syringoma.

A Case for Diagnosis. Presented by DR BENJAMIN LEVINE and DR. N. R. KRUPKIN (by invitation), Cleveland.

G. W., a white man aged 57, has a pruritic, erythematous, generalized eruption of one year's duration. He is well composed and emotionally stable despite the severe itching. He denies having any domestic, economic or personal problems. There is no history of drug ingestion.

The patient is a well developed and well nourished white man who appears his stated age of 57 years. The color of the mucous membranes is normal. Large, diffuse areas of chronic dermatitis cover nearly all parts of the body within his reach, including the face, neck, chest and abdomen, upper extremities, dorsa of the hands, anterolateral surfaces of the thighs and knees, gluteal surfaces and the lumbosacral region. The process is quite symmetrical. Only the inaccessible portion of the back appears quite normal.

The dermatitis is characterized by large, diffuse areas of erythema. The involved areas are very dry, scaling and lichenified. The elementary lesion is a dark red, waxy papule, which varies from 1 to 3 mm. in diameter. The papules are arranged in closely packed parallel bands, which run in the axis of the limbs. This arrangement is particularly noted on the upper extremities and the chest. The lesions on the dorsa of the hands are larger, flatter and gray. The entire bearded area of the face is diffusely involved, while smaller, circumscribed patches are present over the central portion of the face.

Results of examination of the urine were normal. A serologic test of the blood gave a negative reaction. A complete blood count showed the following results: 3,940,000 red blood cells, 5,550 white blood cells and a differential count of 59 polymorphonuclear leukocytes, 7 monocytes, 27 lymphocytes, 6 eosinophils and 1 basophil. The sedimentation rate was 68 mm. in one hour, while tests of bleeding and clotting time gave essentially normal results.

Histologic examination showed moderate hyperkeratosis throughout the section. The granular layer was diminished and in some areas completely absent. The prickle cell layer showed areas of increased thickness with adjacent atrophy. The basal layer was essentially intact, except for a pronounced amount of interstitial edema. The coil glands exhibited atrophic changes. There were a considerable number of pigment-laden cells in the upper part of the corium. In the lower portion of the corium there was a nodule made up of lymphocytes and a few pale-staining cells, with the addition of pigment-laden cells. Adjacent to this nodule there was considerable fibroblastic proliferation. The blood vessels in this area had undergone changes consisting in thickening of their walls, with considerable fibroblastic proliferation.

DISCUSSION

DR. HERMANN PINKUS, Monroe, Mich.: I think before one decides whether this case is lichen ruber moniliformis one has to agree on what that diagnosis means. The peculiar thing, which one observes if he looks through the first description by Kaposi of lichen moniliformis and then the half dozen or so later publications up to Wise and Rein's paper, is that each author claims that his case is the only one that resembles Kaposi's and that all the other cases published were of something else. It is probable that there are cases of what is now called lichen planus which have an arrangement in beads and strands and to which probably the name of lichen ruber or lichen planus moniliformis might be applied. However, from what I have seen, I believe that what Kaposi published a report of probably was not a case of lichen planus at all. At that time this concept was not too well developed, and Wise and Rein definitely state that their case was not a case of lichen planus but was some new and unknown disease to which they gave the name of morbus moniliformis lichenoides. I think Dr. Rein is here in the audience and can say best whether the present case falls into the concept of this disease. The only case of lichen ruber moniliformis that I have ever seen looked very much different. In that case the diagnosis was made by my father, and he also said that the case was the only one that resembled the first one of Kaposi's. I don't know. I think that the case that he diagnosed as such certainly was not lichen planus but represented a combination of traumatisms in a girl who had epidermolysis bullosa and probably some unknown itchy skin disease. The case that was presented here today I am sure is not lichen planus. The histologic picture looks, as much as I can say, similar to that Drs. Wise and Rein have described in their case, and it is quite possible that the disease falls into the category of morbus moniliformis lichenoides.

DR. CHARLES R. REIN, New York: There is very little to add to what Dr. Pinkus has said. Clinically the condition does look like morbus moniliformis ruber, particularly on the upper extremities. I do feel that this case is a little different from others that have been reported. The lesions on the legs do not have the small beadlike arrangement.

DR. RICHARD S. WEISS, St. Louis: I should like to agree with the diagnosis. The disorder is lichen; it is moniliform, but it is not ruber.

Multiple Idiopathic Hemorrhagic Sarcoma of Kaposi Limited to Toes. Presented by DR. IRVING L. SCHONBERG, Cleveland.

Multiple Idiopathic Hemorrhagic Sarcoma of Kaposi. Presented by DR. BENJAMIN P. PERSKY, Cleveland.

T. F., a white man aged 76, presents an eruption on the feet and lower part of the legs, of four years' duration. The primary lesion is a deep-seated nodule. Some of the lesions are red, and others are violet, while still others are mahogany-colored. They vary in size from that of a pea to that of a dime. Interspersed are plaques of tender, indurated skin.

The examination of the urine revealed normal values. The hemogram was normal. The result of the blood Kline test was negative.

Histologic study of a lesion taken from the skin of the left leg revealed the following: Moderate hyperkeratosis was present throughout the epidermis, with slight to moderate acanthosis. The primary pathological changes were seen in the corium. There were a well defined tumor and pronounced interstitial edema, with an infiltration of small round cells and wandering connective tissue cells. Many thin-walled, dilated blood vessels were observed. Within the tumor itself there were lakes of red blood cells. Some of these were engulfed by various-sized cells, some resembling wandering connective tissue cells and others having the shape of spindle cells, which were densely packed. Interspersed between these were numerous spherical, pale cells. Some of these showed deeply stained nucleoli and occasional mitotic figures. New blood vessels were likewise seen in the tumor.

DISCUSSION OF PRECEDING TWO CASES

DR. ROY L. KILE, Cincinnati: I thought I might talk just a minute generally about this disease, which was described in 1879 as idiopathic multiple pigmented sarcoma by Moritz Kaposi, who had seen about 16 cases. The interesting thing about the condition is its exact nosologic position. While the disease is malignant, many patients live for years; others will die in a short period. Kaposi separated it from other sarcomas because of many differences. Where to classify it is a problem. Some classify it as one of the lymphoblastomas, and others, as an infection. There is some evidence that spread of lesions is not due to metastases but rather that there are multiple primary foci of the disease.

About a year and a half ago Pireneau and Grimspan in an Argentine medical journal reported on the use of penicillin in rather large doses in the treatment of three patients, with rather remarkable results. In the uncomplicated disease in the younger patient the response was very good. In the one case on which this therapy has been tried in Cincinnati it has not worked. If the antibiotics are effective, our ideas of this disease will certainly have to be changed.

DR. WILLIAM B. GUY, Pittsburgh: As regards the terminology and classification of this condition, I should like to endorse the suggestion of Dr. Wilbert Sachs that we put it in the group of angioblastomas, including of course the angioendotheliomas and simple angiomas and any other tumor whose stem cell seems to be the angioblast. I think doing so satisfies at least my terminology and classification problem.

Porokeratosis (Mibelli). Presented by DR. H. N. COLE, DR. J. R. DRIVER and DR. H. N. COLE JR., Cleveland.

N. A., a white man aged 65, presents numerous small hard spots on the dorsa of the feet, of 40 years' duration. He states that he has never received arsenicals in any form and, although he is a landscape architect, he denies exposure to arsenical sprays.

Examination shows many pinhead-sized to split pea-sized light brown, hyperkeratotic lesions confined to the dorsa of the feet. These hyperkeratotic plugs have an irregular, rugose surface and when removed leave an erythematous depressed base.

Microscopic examination of a biopsy specimen showed pronounced hyperkeratosis and follicular plugging by laminated keratin. Also, there was decided focal infiltration of lymphocytes.

DISCUSSION

DR. FRED JACOBS, Pittsburgh: I think many of us were surprised at the first sight of this case because the usual textbook picture of the disease is one of a large plaque with an atrophic center. However, the histologic picture, I think, fits into the classification of porokeratosis, with the hyperkeratosis, the acanthosis, the enormous thickening of the granular layer and the mild infiltrate. There were no lesions on the soles or palms, where hyperkeratosis penetrans occurs. It is a rather curious type of disease. We see it but very, very rarely; yet Gilchrist, Rustee and others have reported series of as many as 11 cases. Gilchrist's cases were all in four generations of the same family, that fact indicating a possible hereditary or familial factor. The disease has been reproduced by Becker, and also, I believe, by Rustee, by injection of macerated material, that observation suggesting the possibility of an infectious process, but none of these reports have been conclusive, so that at the present time the condition is a very rare and mysterious disease.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: I should like to challenge the diagnosis rather demurely because I am not sure that I have seen more than one case of porokeratosis. As Dr. Jacobs has said, the classic description was of a plaque with an elevated margin, suggesting the wall of Jerusalem, and microscopically the picture in the present case is not entirely pathognomonic. I was impressed by the discrete excrescences on the feet in an otherwise well, elderly man, and I was also impressed by the peculiar hemangiomas, described as telangiectasia, about the face. Now the microscopic section of tissue which was presented did not show angiomatous features, but I would suggest that this disorder was a form of angiokeratoma.

DR. HERBERT Z. LUND, Cleveland: I wonder whether you have other sections, Dr. Cole, besides those you showed me at the Clinic, because the section shown has a rather oblique cut and I could not pick out the porokeratosis in it.

DR. H. N. COLE, Cleveland: Dr. Lund is our histopathologist. The only section that this patient had that showed the typical lesion was removed. It had the typical picture, with the depression in the center and the wall around it.

DR. ISAAC J. ARNSSON, Buffalo: I want to support the diagnosis of Dr. Brunsting, that this is a case of angiokeratoma. The microscopic slides were typical; they had all the elements of angiokeratoma.

DR. MYER W. RUBENSTEIN, Pittsburgh: The histological section showed dilated lymph vessels, I thought; I interpreted the lesions as keratosis around the orifices of the lymph vessels. I should like to suggest the diagnosis of keratotic lymphangioma.

A Case for Diagnosis. Presented by DR. E. W. NETHERTON, Cleveland.

F. B., a white woman aged 30, presents an eruption of six years' duration. It began as an erythematosquamous and papulovesicular process on the lower portion of the abdomen and then gradually spread to involve most of the body. Papulovesicles, which were described by the patient as the initial lesions, have not been a conspicuous feature of the eruption during the past four years. Pruritus has been a distressing symptom. Since 1945 the patient has noted that her fingers become cyanotic and painful on exposure to low temperatures.

The previous medical history and family history are noncontributory.

There is a symmetric polymorphous eruption involving the neck, chest, abdomen, shoulders, back, arms and thighs. There are large areas of partial depigmentation, scarring and telangiectasia and also small erythematous, scaly plaques. There are numerous small varioliform scars on the upper portion of the back. Small follicular hyperkeratotic papules and spines, as well as foci of perifollicular hyperpigmentation, are present throughout the large pigmented and scarred areas on the trunk. There is scarring, depigmentation and variegated hyperpigmentation on the anterior and lateral surface of each thigh and areas of erythema and telangiectasia on the buccal mucosa.

Wassermann and Kahn reactions of the blood were negative. The hemogram and results of examination of the urine were essentially normal. The sedimentation rate was not significantly elevated.

Microscopic examination of a papular lesion showed hypertrophy of the epidermis. There was hyperkeratosis with spotty parakeratosis. There was a fairly well defined area of necrosis in the midcorium, composed of degenerated collagen and polymorphonuclear leukocytes. There was a nonspecific inflammatory reaction around this area.

Sections from a partially depigmented region showed areas of atrophy of the epidermis and liquefaction degeneration of the basal layer. Beneath these areas there was extensive subepidermal edema and homogenization of collagen in the upper part of the corium. A mild perivascular lymphocytic infiltrate was noted.

Sections from an erythematous, scaly plaque showed changes essentially the same as observed in tissue sections of the second biopsy specimen but differed in that there was more extensive subepidermal edema, homogenization of collagen and follicular plugging.

DISCUSSION

DR. LEON GOLDMAN, Cincinnati: Lichen sclerosus et atrophicus is the main feature, with typical lesions on the trunk, involvement of the genitalia and incidentally involvement of the buccal mucosa. Vesicles and bullae occasionally occur in lichen sclerosus et atrophicus, and in some of our experiments with the hypospray apparatus in patients with lichen sclerosus et atrophicus we have produced bullae very easily. The picture, I think, is changed somewhat because of the associated Raynaud's syndrome; the history indicates that the characteristics did change after the Raynaud syndrome developed. I believe that it is because of this associated vasospastic condition that the patient has had secondary poikilodermatous changes in some of these areas. The biopsy specimen also supports the diagnosis of lichen sclerosus et atrophicus. I should appreciate some remarks about the therapy for this particular disorder.

DR. RICHARD S. WEISS, St. Louis: Assuming that the diagnosis is lichen sclerosus et atrophicus—and I have heard some discussion around the patient that led me to believe that not everyone agreed—I should like to answer Dr. Goldman's question as to the treatment thereof. In a number of cases of lichen sclerosus et atrophicus we have had pretty good luck from treatment with the tocopherols in large doses over quite a long period. I am not sure but that this disease gets well by itself sometimes, and so I can't say whether or not the tocopherols produced the result, but several cases over a period of six months to a year and a half have apparently cleared, very thin atrophic areas being left. I observed one case in a man who had numerous lesions all over his back and chest; under this treatment practically every one of the patches underwent involution.

DR. E. W. NETHERTON, Cleveland: We feel that the histologic changes, as Dr. Goldman has said, are quite compatible with the diagnosis of lichen sclerosus et atrophicus, but clinically the condition certainly does not correspond to any case of lichen sclerosus et atrophicus that I have seen. It has many of the features but is certainly not typical of that disease.

Epidermolysis Bullosa. Presented by DR. NORMAN ASEL, DR. PAUL CHIVINGTON and DR. WILLIAM SPILLER for DR. JOHN E. RAUSCHKOLB, Cleveland.

S. L., a white baby girl aged 10 months, presents a generalized bullous eruption which has been present since birth.

On examination there are observed crusted, denuded areas on the scalp, ears, face neck, arms, trunk, buttocks and lower extremities. The buccal mucosa is also involved. Many of the nails are missing.

Epidermolysis Bullosa Dystrophica. Presented by DR. BENJAMIN LEVINE, Cleveland.

B. W., a white woman aged 23, presents vesicles and blebs on the ankles, elbows, knees and phalanges. Accompanying this disorder is a dystrophy of all nails. The patient states

that this condition has been present since shortly after birth and notes that trauma plays a major role in precipitating new lesions.

The patient's father and one of four siblings have the same condition, to a lesser degree.

DISCUSSION OF PRECEDING TWO CASES

DR. LOUIS A. BRUNSTING, Rochester, Minn.: The diagnosis in these cases is self evident, but they add to the wonderful panorama of hereditary disturbances of the skin that we have seen. I have never attended a medical meeting where more examples of hereditary dystrophies and disturbances were presented. I think in the field of dermatology and in the field of ophthalmology there are unexcelled opportunities for recording hereditary disturbances, and we don't make the most of them. A geneticist will readily list for you the criteria that are necessary for the drawing of conclusions in regard to the types of hereditary patterns that exist for these diseases. If those things are mentioned on the history, well and good. If they are not mentioned, the patient and his research value toward genetics are lost. For instance, we are well acquainted with the relation of consanguinity to some of these diseases, but usually we don't inquire as to the relationship of the patient's parents or grandparents, whether or not they are cousins or have a common name. In listing these people, we might go into the background of the family names. Johnson and Test, as reported in their admirable paper a few years ago in the ARCHIVES, followed cases of epidermolysis bullosa through seven and eight generations, some 365 persons, and found that the history went back before the year 1800 in this country.

Now the hereditary pattern of epidermolysis bullosa varies, not necessarily according to whether it is the simple or the dystrophic form. There may be varied patterns to a single disease with clinical classifications as alike as this one. When we consider ectodermal dysplasias, for instance, from the field of ichthyosis to ichthyosiform erythroderma and dysplasias of the hidrotic and anhidrotic types, we will find varied genetic patterns. I think one function that we can serve in regard to these rare conditions is to establish a genetic pattern. No one has satisfactorily explained the vulnerability of this skin to trauma. We casually say that there is some disturbance of the elastic tissue, but is there? In a condition in which there is a profound disturbance of the elastic tissue, such as pseudoxanthoma elasticum, we see none of this vulnerability. In diseases of the binding tissue otherwise, such as the collagen diseases, rarely in lichen sclerosus, we do observe this vulnerability to trauma.

I perhaps was asked to open this discussion because I was interested in the phase of the vulnerability of the skin and the blistering reaction that occurs in some patients with porphyria. I think the term epidermolysis bullosa is a poor one to use, just as the term hydroa is a poor one to use. In porphyria as it occurs for the first time in adults, there is a hyper-reactivity of the exposed skin to sun and a vulnerability to trauma. In fact, the latter sign may be the first one the patient has noticed. The patient hurts himself—his hand in his work or against some object—a small hematoma occurs, and a blister may occur two or three days later; that development may be the first sign of porphyria. In studying such patients we have been impressed by the hereditary pattern. There is a familial incidence. It is different from that in acute porphyria and somewhat similar to that which is seen in the rare form of porphyria called congenital porphyria. In all those cases that we have studied there has been some provocative agent responsible for the development of the symptoms for the first time in adult life, and these agents have all been centered on the liver. In a series of 20 cases, that we have observed —four that have been reported and 16 soon to be reported—14 of the patients were alcoholics. In two of them syphilis also occurred. Three of them were diabetics, and one of the diabetics had a history of alcoholism to a mild degree. The other two diabetics had neuropathies. In one case, the most profound example, we found an enlarged liver, a sulfobromophthalein dye retention of grade 3 and results of zinc sulfate and thymol turbidity tests all indicating a severe degree of hepatic dysfunction, without any adequate explanation. Then the patient came forward with her story that some 20 years before she had been given drop medicine and had taken potassium arsenite (Fowler's) solution, not by the drop but by the teaspoonful, and still she showed none of the usual signs of arsenism as we recognize them on the skin. However, it is well known that there is a delayed effect on the liver. Cirrhosis will follow many years after

the ingestion of these inorganic salts of arsenic. Two or three of the other patients had taken sedatives, and sedatives of the sulfonyl type, barbiturate group, are known to precipitate symptoms of porphyria. So in these cases the single factor which precipitated the blistering reaction or vulnerability of the skin was something operating indirectly through the liver. Whether porphyrins were projected into the circulation and thus made the skin sensitive to light and to trauma we don't know, or whether or not some unknown porphyrin or photosensitizer was projected that way, or whether there was some indirect mechanism on the enzyme system of the skin which has to do with the binding quality. I think that we should direct our further efforts toward the study of these cases, as in epidermolysis bullosa, not so much to the static study of fixed tissue sections and the interpretation of tinctorial reactions as perhaps toward this newer field of enzyme mechanisms and how responsible they are for maintaining the skin in a normal state.

Dermatitis Herpetiformis: Response to Nicotinic Acid Therapy. Presented by Dr. H. H. Johnson and Dr. G. W. Binkley, Cleveland.

Because of the presence of late latent syphilis penicillin therapy was given; it was found ineffective for the dermatitis herpetiformis. Pyridoxine was given for a period of two weeks and found to be of no value. Sulfapyridine was given for a week and adequately controlled the symptoms. However, treatment with it was not continued when it was found that the administration of nicotinic acid, 0.1 Gm. four times daily, was equally efficient. Therapy with nicotinamide in the same dose as nicotinic acid does not control the symptoms. This patient has taken nicotinic acid since October 1947 and was asked to discontinue the medication on April 21, 1950.

Amyloidosis Cutis. Presented by Dr. H. N. Cole, Dr. J. R. Driver and Dr. H. N. Cole Jr., Cleveland.

H. D., a white man aged 44, presents an eruption limited to the lower legs, lower part of the back and upper arms, of eight years' duration.

Examination reveals no abnormalities other than the skin lesions, which consist of firm elevated, hyperkeratotic, hyperpigmented, pinhead to split-pea-sized folliculopapules. One hour after the intravenous administration of congo red there was 28 per cent absorption.

Histologic examination of a lesion taken from the lower leg showed foci in the superficial part of the corium in which the fibrillar structure was lost. In these foci the normal tissue appeared to be replaced by an amorphous, granular material, which possessed an affinity for metachromatic staining.

DISCUSSION

Dr. Leon Goldman, Cincinnati: Our pathologist has been interested in what is called amyloid in the skin, which is a general group of perhaps many different chemicals. He is concerned with the possibility, through histochemical studies, of determination of the relationship to hyalin. Another thing—the intradermal congo red test is not as easy a test as it always seems, and we are trying to develop the use of congo red by the hypospray, so that it can be squirted into the skin and the coloration of the papules more easily outlined.

Dr. Samuel Goldblatt, Cincinnati: We have been observing simultaneously two cases of localized amyloidosis, localized to the lower legs, much more extensive than the condition in the patient presented here today. In both of these cases, however, the Bennhold test intravenously gave completely negative reactions, even after 24 hours, that fact indicating that the condition is a completely local skin phenomenon. The question in today's case is what happened to the 28 per cent of the congo red that was injected that did not show up in the serum, whether or not this patient has some systematized amyloidosis, with consequent absorption of some of the congo red. We know, of course, nothing about the actual chemistry of amyloid or how it is deposited. I was prompted to take one of these patients and first inject congo red into the entire area, in order to prove that the amyloidosis actually existed in these spots, and then inject 1 to 2 mg. of thyroxin into the lesions directly. Doing so is not an easy procedure. Making an intradermal injection into an amyloid lesion almost requires a pile driver. However, very

shortly, within one or two weeks thereafter, within the area that had received the injection the lesions began to lose color and began to get flatter and finally flaked off, leaving a perfectly normal skin.

In the second case, in order to test the efficacy of the thyroxin, we gave fairly large doses intramuscularly. Both of the patients had complained of very severe itching, and in both the condition was of 10 to 20 years' duration. In the case in which the material was injected intracutaneously the itching ceased in the area which had received the injection. In the case of the patient who received his thyroxin intramuscularly, after a period of two weeks the itching had stopped, although there was no change in the lesions at all except that the entire skin, which was previously extremely firm and could hardly be depressed, became quite soft. The lesions, however, retained their scaliness and their nutmeg-grater-like shape and feel, and they have so far not been influenced.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: It is a surprising thing that amyloid deposits do not occur more in patients with so-called secondary amyloidosis. Those that occur in the skin are like those you saw today, the lichenified type, or are observed as masses of amyloid, either in solitary nodules or in cases of systematized amyloidosis. In studying the reports of those who have investigated the chemistry of amyloid, it is interesting to note how the substance first got its name. I had not given the matter much thought, but the name came from a similarity to starch—similarity, of course, in staining reaction—and its rather peculiar metachromatic response to certain stains is the only way that pathologists have to identify it today. In that respect amyloidosis has some similarity to hyaline deposits and fibrinoid deposits, and in a way is somewhat similar to the mucin changes that we see in lichen myxedematosis.

DR. ARTHUR SCHILLER, Detroit: The statement was made that it took the pressure of a pile driver to put the medication in situ. I just wonder whether it was thyroxin that caused a change in the amyloid tissue or whether any other medication, or even water, put in under such pressure might not give the same effect.

DR. SAMUEL GOLDBLATT, Cincinnati: We injected both procaine and congo red under the same type of pressure, without producing any change.

Chronic Discoid Lupus Erythematosus. Presented by DR. NORMAN ASEL, DR. PAUL CHIVINGTON and DR. WILLIAM SPILLER for DR. JOHN E. RAUSCHKOLB, Cleveland.

Systemic Lupus Erythematosus. Presented by DR. JOHN R. HASERICK, Cleveland.

B. P., a white woman aged 32, is presented to show the value of the plasma L.E. test in cases of disseminated lupus erythematosus, particularly in those not having associated skin lesions.

The patient was well until 1942, when she noted the onset of mild arthralgia involving the hands, knees and ankles. Mild swelling of the joints of the fingers was present. The symptoms remained unchanged until one year prior to admission, when there was a pronounced exacerbation of joint symptoms. The patient was hospitalized for five months in 1949 because of tachycardia, bilateral pleural effusions and pericardial effusion. Laboratory studies revealed moderate anemia, leukopenia and an increased sedimentation rate but no L.E. cells. The patient was transferred to Mount Sinai Hospital in New York, where the same observations were demonstrated except that L.E. cells were found. In November 1949, she became severely ill and the condition appeared terminal. She was treated with cortisone for seven weeks, followed by ACTH therapy, until Jan. 3, 1950. She was referred to the Cleveland Clinic in March 1950.

Laboratory data revealed a positive reaction in the plasma L.E. test, hemoglobin of 11 Gm. per 100 cc., 2,800 white blood cells and a decidedly increased sedimentation rate.

Physical examination revealed a temperature of 99.2 F.; pulse rate, 112, and blood pressure, 104/64. General physical examination revealed an essentially normal condition. There was no evidence of any abnormality in the skin.

After ACTH therapy was discontinued the patient's condition entered an incomplete remission. She remained afebrile and complained only of mild stiffness in the neck. She began to menstruate for the first time in several months in February. She menstruated normally again one month later. In spite of the clinical remission, laboratory evidence for continued

activity included leukopenia, a strikingly increased sedimentation rate and a positive reaction in the plasma L.E. test.

Chronic Systemic Lupus Erythematosus. Presented by Dr. John R. Haserick, Cleveland.

The patient was first seen at the Cleveland Clinic in 1939 because of convulsions. A diagnosis of idiopathic epilepsy was made at that time. One month later she was admitted to the Cleveland Clinic Hospital with pleurisy and effusion of the left side of the chest. History of rheumatic pains for many years was considered in arriving at a diagnosis of rheumatic pleural effusion. The patient remained comparatively well until 1949, when there was an increase in the number and severity of her grand mal seizures. In addition, pronounced swelling of the ankles and fingers occurred, and because of these symptoms the patient was hospitalized in the fall of 1949.

Physical examination revealed a very faint erythema of the cheeks, with a macular pigmentation. Swelling of the proximal interphalangeal joints, clubbing of the fingers and moderate edema of the ankles were present.

A blood count gave the following results: hemoglobin, 10.5 Gm. per 100 cc., and white blood cells, 4,250. The sedimentation rate (Rourk-Ernstene) was strikingly increased. Urinalysis revealed occasional traces of albumin but an otherwise normal condition. The plasma L.E. test gave a positive reaction.

Treatment with testosterone cyclopentyl-propionate was begun in February 1950. Administration of cortisone, 100 mg. weekly, was begun March 21, 1950.

There has been a definite increase in the general well-being of the patient; however, as yet there has been little objective improvement.

DISCUSSION OF PRECEDING THREE CASES

Dr. Richard S. Weiss, St. Louis: The second case of chronic systemic lupus erythematosus is exceedingly interesting and especially so to me because of the fact that there was a diagnosis of chronic idiopathic epilepsy. Just last week my attention was called to a patient in Barnes Hospital, a young woman who had had epilepsy from childhood and who had been treated with mesantoin® (3-methyl-5,5-phenylethylhydantoin) over a period of several years who suddenly got sick and was sent into the hospital with a diagnosis of possible mesantoin® poisoning. She had fever, arthralgia, moderate but not too severe leukopenia and some pleuritic symptoms and was still taking mesantoin.® That therapy was stopped, and she did not improve very rapidly. There was a faint blush over both cheeks but nothing else to suggest disseminated lupus erythematosus. However, the Barnes-Moffatt test gave repeatedly positive reactions. A further study of the case over the next few days convinced us that it was one of disseminated lupus erythematosus. The patient presented today has a similar history of idiopathic epilepsy. I don't know whether she had been treated with mesantoin,® but it is quite likely she had been. This observation leads us to make further experiments with the L.E. phenomenon by testing out 30 to 40 epileptic patients who are under treatment with mesantoin.® We don't know whether or not that drug is a toxin that might produce the L.E. phenomenon or a substance which might stimulate the production of the toxin, if you want to call it that, that produces the L.E. phenomenon. We have to make tests on these persons to increase our number of controls. I think that is a very important thing to do, and we are going to do it and report on it a little later.

Hyperkeratosis Congenita Generalisata cum Cornubus. Presented by Dr. J. J. Stewart, Dr. J. G. Thomsen and Dr. R. K. Gardner for Dr. H. N. Cole and Dr. J. R. Driver.

R. G., a white man aged 34, presents a skin condition which he states has been present since infancy. He dates his present illness back to the age of 17, when he manifested papulopustules over the abdomen, axillas, thighs, back, scalp and external genitalia. These lesions were symptomless but would slowly enlarge, becoming frankly purulent and later verrucous and hyperkeratotic. These lesions healed with scar formation. New lesions have continued to appear, especially during the summer. The patient has recently had an exacerbation of numerous papulopustular lesions over the legs, forearms and back.

In January 1946 a diagnosis of squamous cell carcinoma of the scrotum was made. The growth was surgically excised.

The face presents numerous comedos and scars. Over the scalp there are many depressed scars. On the back are numerous discrete papulopustules with areas of scarring and hyperpigmentation interspersed. On the right nipple and areola is a hyperkeratotic verrucous lesion with an erythematous base. The penis, anterior aspect of the thighs and the ankles are studded with similar lesions.

The hemogram yielded normal results, with the exception of mild eosinophilia. Cultures of purulent material taken from an active lesion grew out Staphylococcus aureus. Cultures for fungi have been repeatedly negative. Urinary excretion of 17-ketosteroids was within normal limits.

Histologic examination of skin sections showed chronic dermatitis with verrucous hyperplasia and hyperkeratosis.

DISCUSSION

DR. LOUIS A. BRUNSTING, Rochester, Minn.: The thing that intrigues me about this case is the cum cornubus aspect. Dr. Levine asked me to open the discussion on this patient, and so I looked him over rather carefully, but I was not able to satisfy myself as to the essential nature of his troubles until I saw the scarring from his acne. There were not only the comedos but also the double comedos widespread over his trunk, especially on the upper part. The condition reminded me of a number of patients with pyoderma whom we have seen; in them the disorder began as fulminating acne, and then for some reason or other the unusual areas of the skin became involved with this pyogenic process and hyperkeratoses. The congenital aspect of the history, as I learned on inquiring of the patient, probably has to do with a skin disorder he had in infancy, which he told me was a form of eczema.

DR. H. N. COLE, Cleveland: Milian wrote an article (in Darier and others: La Nouvelle Pratique Dermatologique, vol. 6, Paris, Masson & Cie, 1936, p. 689) on the precancerous nevoid erythrokeratodermas. One of these he put down as epidermal dysplasia of the small papule type. The second form that he described was a diffuse form, and he reported the case of a patient who had been affected when he was about 6 months old and had had the condition his entire life. Our patient had had the disorder at least as early as 2 years of age. The patient of Milian's had been seen by Darier in 1911, and Darier had made a report on it (*Bull. Soc. franç. de dermat. et syph.* **22**:252, 1911) at that time. This patient had a diffuse keratotic type of erythroderma, involving practically all the body except the face, the palms of the hands and the genitalia, and in some places as time went on these lesions not only had become papules but even had formed cutaneous horns. When Milian made his report on the case he stated that some of these cutaneous horns had even become as long as 10 cm. and that because of the pressure of the patient's clothing they had turned over and pressed into the skin. One area on the dorsum of the foot, after trauma degenerated and developed into a squamous cell carcinoma. Another area on the anterior aspect of the shoulder likewise degenerated and developed into squamous cell carcinoma.

This patient of ours does not show as many lesions now as he has had, because large plaques have been treated with X-ray spray. Curiously enough, Milian reported that he and his associates did the same thing with their patient and removed many of the smaller areas likewise. Our patient acquired a large squamous cell carcinoma on the inside of the thigh several years ago. It was removed, with removal of the lymph nodes at the same time, and there has been no aftermath as yet.

Lupus Vulgaris. Presented by DR. NORMAN ASEL, DR. PAUL CHIVINGTON and DR. WILLIAM SPILLER for DR. JOHN RAUSCHKOLB, Cleveland.

A Case for Diagnosis: Mycosis Fungoides with Infiltrated Patches Limited to Legs, Present for Seven Years? Presented by DR. NORMAN ASEL, DR. PAUL CHIVINGTON and DR. WILLIAM SPILLER for DR. JOHN E. RAUSCHKOLB, Cleveland.

Parapsoriasis en Plaque: Patient Under Observation for Ten Years; Condition Unchanged. Presented by DR. H. N. COLE, DR. J. R. DRIVER and DR. H. N. COLE JR., Cleveland.

A Case for Diagnosis: Pityriasis Lichenoides Chronica? Presented by DR. BENJAMIN LEVINE and DR. GEORGE H. CURTIS, Cleveland.

Pityriasis Rubra Pilaris, Improved After Treatment with Vitamin A. Presented by DR. GEORGE H. CURTIS, Cleveland.

Pemphigus Vulgaris. Presented by DR. E. W. NETHERTON, Cleveland.

Pemphigus Vulgaris. Presented by Dr. Norman Asel, Dr. Paul Chivington and Dr. William Spiller for Dr. John E. Rauschkolb, Cleveland.

Xanthoma Diabeticorum. Presented by Dr. J. J. Stewart, Dr. J. G. Thomsen and Dr. R. K. Gardner for Dr. H. N. Cole and Dr. J. R. Driver, Cleveland.

Xanthoma Tuberosum Multiplex. Presented by Dr. J. J. Stewart, Dr. J. G. Thomsen and Dr. R. K. Gardner for Dr. H. N. Cole and Dr. J. R. Driver, Cleveland.

Necrobiosis Lipoidica in a Nondiabetic. Presented by Dr. George H. Curtis, Cleveland.

Mycosis Fungoides Resembling Psoriasis. Presented by Dr. J. J. Stewart, Dr. J. G. Thomsen and Dr. R. K. Gardner for Dr. H. N. Cole and Dr. J. R. Driver, Cleveland.

Mycosis Fungoides, Promycotic. Presented by Dr. E. W. Netherton, Cleveland.

A Case for Diagnosis: Generalized Pruritus. Presented by Dr. Norman Asel, Dr. Paul Chivington and Dr. William Spiller for Dr. John E. Rauschkolb, Cleveland.

A Case for Diagnosis: Clinically Parapsoriasis, Histologically Bowen's Disease. Presented by Dr. E. W. Netherton, Cleveland.

Dermatomyositis. Presented by Dr. J. J. Stewart, Dr. J. G. Thomsen and Dr. R. K. Gardner for the Department of Internal Medicine, University Hospitals, Cleveland.

Systematized Scleroderma. Presented by Dr. Frank M. McDonald, Akron, Ohio.

Scleroderma, Treated with Cortisone. Presented by Dr. John R. Haserick, Cleveland.

Lichen Nitidus. Presented by Dr. J. J. Stewart, Dr. J. G. Thomsen and Dr. R. K. Gardner for Dr. H. N. Cole and Dr. J. R. Driver, Cleveland.

A Case for Diagnosis: Amyloidosis Cutis? Presented by Dr. Frank M. McDonald, Akron, Ohio.

CHICAGO DERMATOLOGICAL SOCIETY

Theodore Cornbleet, M.D., *President*

James R. Webster, M.D., *Secretary*

May 17, 1950

A Case for Diagnosis: Dermatitis Herpetiformis? Pemphigus? Treated with Progesterone. Presented by Dr. James H. Mitchell.

Mrs. N. S., aged 71 years, was first seen by me on Jan. 4, 1950 with an extensive bullous eruption. The eruption had begun in October 1949 as an erythematous eruption, extremely pruritic, chiefly over the upper part of the back and to a lesser degree on the chest. The hair had been dyed for many years. Bullae had recently begun to appear, and the patient described them as being as large as hen's eggs.

The patient is obese. On the occasion of her first visit she had a generalized bullous eruption. Sulfapyridine was prescribed, and on January 8 the patient was admitted to the Presbyterian Hospital. The iodine test gave negative results after 18 hours. The eosinophil count of the peripheral blood was 15 per cent and in the content of the bullae, 20 per cent.

After no progress had been made as a result of therapy Dr. Samuel Taylor suggested that one of the 28 steroids now in use might be tried and suggested progesterone (proluton®). Thereupon the patient was given 100 mg. of progesterone daily for some weeks and was discharged from the Presbyterian Hospital on February 21, practically clear.

The patient was next seen on March 9, with large erythematous relics but free from bullae. There were groups of milia-like lesions on the extremities which later disappeared.

On March 29 the patient appeared with an erosion on the lower part of the right leg, apparently a relic of a ruptured bullae. On April 26 she had numerous small bullae. Treatment was begun with the injection of 10 mg. of progesterone. This dose was repeated April 27 and 28 and May 1, 3, 4, 8, 10, 12 and 15.

Examination on May 15 disclosed no sign of bullous activity.

DISCUSSION

Dr. Ruben Nomland, Iowa City: I should like to add a third diagnosis, as I think the condition is bullous lichen planus. To make a diagnosis of bullous lichen planus one must take the biopsy specimen from a nonbullous lesion. I am sure that if you take a specimen from the lesion on the back of the hand you will observe in it a very good example of lichen planus.

Dr. Michael H. Ebert: I saw this case with Dr. Mitchell. It looked like typical pemphigus as far as I could see except that the patient did not have lesions in the mouth. She was covered with bullae. As far as these little milia-like lesions are concerned, some of you will recall that Dr. Omens and I showed a case of a man who had a number of these lesions after a burn on the hand. There was much discussion as to what they were. Later on they all disappeared.

So that occurrence is not unusual. In the case presented today the treatment has been nothing short of miraculous in its effect on the bullous, pemphigus-like lesions.

DR. JAMES H. MITCHELL: I have not seen milia-like lesions in lichen planus. The lesions came on in the course of a few days. I have no idea of what this case is. Do not ask me what the rationale of the treatment is. I have been in close touch with Dr. Samuel Taylor, who supplied the ACTH for three cases of mine. Two patients with mycosis fungoides and one with exfoliative dermatitis treated with ACTH are now dead.

NOTE.—The patient presented made a complete recovery and had no sign of further activity at last observation.

Xanthoma Diabeticorum. Presented (by invitation) by DR. MALCOLM C. SPENCER, Danville.

W. F. B., a white man aged 34, was admitted to Danville Veterans Administration Hospital Aug. 4, 1944 and discharged May 6, 1950. The admitting diagnosis was schizophrenic reaction of hebephrenic type, chronic and severe. This disease developed after the patient had spent a year or so in the armed services. He had had no foreign duty. There was no history of a similar disorder in any other member of the patient's family. His prognosis until recently was considered poor. He was so uncooperative during the first part of his hospitalization that no shock therapy could be given. His treatment, for the most part, has been institutional care, but with the improvement of his mental state which has been correlated with the improvement in his cutaneous manifestations occupational therapy and psychologic interviews have been carried on.

This patient was first seen by me on Jan. 20, 1950. Because of the lack of mental contact, a definitive history was unobtainable. Review of his hospital record indicates that no cutaneous lesions were noted in 1944, the time of his admission, or on subsequent physical examinations until approximately six months before he was first seen by me. His admission weight in 1944 was 219 pounds (99 Kg.). His weight in January 1950 was 231 pounds (105 Kg.).

A general medical examination on January 20 revealed an obese white man of the stated age, obviously mentally ill, with hallucinations and lack of mental contact with the surrounding environment. The blood pressure was 160/80. The general medical examination revealed no abnormality except for the pronounced obesity, the distribution of which was suggestive of that in the Fröhlich syndrome.

On dermatologic examination it was seen that scattered over most of the extensor areas of the cutaneous surfaces—that is, elbows, posterior axillary folds, knees and buttocks—were papules and nodules of a firm consistency and yellowish tinge. These were not associated with an inflammatory base. They measured from 0.5 to 1.0 cm. in diameter. Mucous membranes were normal.

The weight was 231 pounds and the height, 68 inches (175 cm.). A chest roentgenogram revealed no abnormality; a roentgenogram with a lateral view of the skull showed the sella turcica to be definitely smaller than the average normal. The electrocardiogram had a normal tracing. The blood pressure was 160/80. Weights were as follows: January 20, 235 pounds (106.6 Kg.); March 1, 185 pounds (83.9 Kg.), and May 1, 175 pounds (79.4 Kg.).

It became apparent after approximately one month that the cutaneous lesions were becoming smaller, and of interest was the improvement in the patient's mental picture which seemed to correlate the improvement in his cutaneous lesions. After a period of two months he was given free run of the hosiptal grounds and became interested in occupational therapy. Improvement has continued to the point that attending psychiatrists felt that a 90 day pass from the hospital was indicated. This turn of events is in contrast to the prognosis which was previously entertained and presented to the patient's immediate family, that institutionalization would always be necessary.

The standard Kahn test gave negative reactions. Results of a complete blood count were as follows: hemoglobin, 16.4 Gm.; red blood cell count, 6,270,000; white blood cell count, 9,200, with 59 neutrophils, 28 lymphocytes, 3 monocytes and 3 eosinophils.

Periodic routine urinalyses have had consistently normal results. The blood sedimentation rate was 15 mm. per hour. Blood chemistry determinations on January 27 were as follows: protein, 6.6 mg.; albumin, 3.9 mg.; globulin, 2.65 mg., and cholesterol 387 mg. per 100 cc.,

with cholesterol esters, 207 mg., for a ratio of 53 per cent. On February 23, approximately one month after the patient was placed on an 800 calory diet, the determinations were as follows: cholesterol, 114 mg. per 100 cc., with cholesterol esters, 48 mg. On March 1 cholesterol measured 120 mg. per 100 cc., and on March 29, cholesterol was 109 mg. per 100 cc., with cholesterol esters, 87 mg., for a ratio of 79.8 per cent.

Glucose tolerance testing on January 24 had the results shown in the table.

Results of Glucose Tolerance Tests

	Blood Sugar, Mg./100 Cc.	Sugar in Urine	Reaction for Acetone in Urine
Fasting	132	None	.....
After Glucose			
½ hr	225	Less than 0.5%	.....
1 hr	241	5%	Negative
2 hrs	241	5%	Negative
3 hrs	167	3%	Negative

On March 29 the fasting blood sugar was 95 mg. per 100 cc.

Biopsy of a section taken from a lesion on the buttocks revealed the epidermal layer to be thin and sharply demarcated. In the subepidermal layer and extending into the depths of the corium were groups of polygonal cells with vacuolated cytoplasm. The nuclei of these cells were uniform in size and shape.

The patient was placed on an 800 calory diet on January 25. On April 21 he was placed on a 1,500 calory diet. Thyroid extract, 1 grain (60 mg.) three times a day, has been taken since February 15. Supplementary vitamin therapy in the form of multiple vitamin preparations has been given throughout the course.

DISCUSSION

DR. MALCOLM SPENCER, Danville (by invitation): I should have mentioned on the protocol that the results of liver function tests were normal. This case has created a good deal of interest because the patient had very severe schizophrenia. He was so uncooperative that shock therapy could not be given. It was of a great deal of interest that coincidentally with the improvement in the skin his mental picture improved to such an extent that he is now on leave from the hospital. That is why it is possible to present him today.

Another point of interest has been the following of this patient's blood cheimstry with a new form of microanalysis for fat recently described by K. K. Jones (*Science* **3**:9-10 [Jan. 6] 1950). Fo the last three months I have been working with this method. It is very simple and a very basic type of determination that is dependent entirely on the physical property of the fatty acids and nonsaponifiable materials forming figures on a monolayer of piston oil that has been specially treated. The method is so fine that it is possible for one to determine the fatty content of even one comedo. My associates and I hope to follow clinical cases with this determination.

Dermatitis Herpetiformis: Subungual Hemorrhage Following Sulfapyridine Therapy.
Presented by DR. F. E. SENEAR and Staff.

DISCUSSION

DR. THEODORE CORNBLEET: This man's nails were flat—I would not quite call them spoon nails. My associates and I have been able to show that some people with this kind of nails have lengthened prothrombin times. If this man does, it is possible that sulfapyridine could account for this change in his blood.

Scleroderma: Parallel Bands (Coup de Sabre Type) on Left Side of Forehead.
Presented by DR. JAMES H. MITCHELL and DR. HARRY R. FOERSTER, Milwaukee.

DISCUSSION

DR. LOUIS RUBIN: In the group we studied at the University of Chicago one patient had parallel bands on the skull, as this patient has. There was one 12 year old girl who had multiple

areas of morphea on the trunk, an observation which seemed to indicate that these bands on the skull are definitely related to morphea. This girl also had a sister, 6 years of age, with typical morphea on the trunk.

DR. HARRY R. FOERSTER, Milwaukee: I suggested to Dr. Mitchell that he present this patient because of the similar case he showed at the last meeting. Two cases of scleroderma of the en coup de sabre type, each with roentgenograms revealing no abnormality, are worth seeing even though they offer nothing from the therapeutic angle. The condition in this patient is very likely a trophoneurosis. We have recently observed response in several cases of localized scleroderma to treatment with dihydrotachysterol (hytakerol®), which result lends support to consideration of endocrine factors in the etiology. I would, however, advise against such treatment in a patient of this age (5½ years).

Granuloma Annulare. Presented by DR. D. OMENS and (by invitation) DR. H. OMENS and DR. D. MUSGRAVE.

L. B., a 6 year old Negro boy, first noticed a small "spot" over the dorsum of his left foot three years ago. This lesion has gradually enlarged until at present it is slightly larger than a half-dollar, with a relatively depressed center and an elevated roller border. A similar smaller lesion is present over the medial surface of the left knee. There are no subjective symptoms.

A microscopic section is presented.

DISCUSSION

DR. RUBEN NOMLAND, Iowa City: This case brings up a problem that has been discussed several times before this Society—granuloma annulare that is typical clinically but not microscopically. In my experience about 50 per cent of persons with granuloma annulare do not have the typical microscopic features described in the textbooks. Second, those that do have a typical textbook picture of necrobiosis of the collagen tissue all have fatty infiltration surrounding the necrotic areas as shown by frozen section and stains with sudan III. In many ways the fat infiltration resembles that of necrobiosis lipoidica diabeticorum. I do not believe that if fat stains had been made in this case they would have shown much fatty infiltration.

DR. M. R. CARO: I think it should be mentioned that it requires more than cutting more deeply through the block to make the diagnosis of granuloma annulare. If the lesion is fully developed you do not have to cut very deeply into the block to reach the diagnostic necrobiotic changes that are surrounded by a zone of histiocytic cells.

A Case for Diagnosis: Blastomycosis? Presented by DR. THEODORE CORNBLEET and (by invitation) DR. H. SCHORR and DR. S. BARSKY.

Systemic Blastomycosis. Presented by DR. D. OMENS, DR. JAMES R. WEBSTER and (by invitation) DR. H. OMENS and DR. S. BARSKY.

DISCUSSION OF PRECEDING TWO CASES

DR. F. R. SCHMIDT: For the case of generalized blastomycosis I should like to suggest a new form of treatment as used in South America. I saw two patients who apparently had recovered and had remained free from evidence of the disease with the following treatment: first, a daily intravenous infusion of 1 per cent strong iodine (Lugol's) solution is given, and, second, a vaccine made from cultures of the lesion is used along with large doses of a sulfonamide and ascorbic acid. This treatment is repeated for several courses.

DR. M. R. CARO: I should not like to see the first case go into the literature as an unchallenged case of blastomycosis. The fungus was not found on direct examination. The histologic section was not at all acceptable for blastomycosis. There are no giant cells present, and the spores of Blastomyces were not found. I think the section showed the features of an inflammatory granuloma, much more acute than is seen in blastomycosis. Histologically and clinically I do not believe the case is one of blastomycosis.

DR. A. L. WELSH: I should like to suggest a method for helping to find Blastomyces in some of these lesions. The sponge biopsy technic has been very helpful in some cases my associates and I had recently which did not have little pustules where we would ordinarily look for the organism.

Familial Hereditary Hemorrhagic Telangiectasia in a Negro. Presented by DR. JAMES R. WEBSTER, DR. S. M. BLUEFARB and (by invitation) DR. S. BARSKY.

DISCUSSION

DR. S. M. BLUEFARB: The only reason for presenting this case is the rarity of this disease in the Negro. Dr. Schwartz of the hematology department tells us that this is only the second case he has ever seen in a Negro.

Tuberculosis Cutis? Sarcoid? Presented by DR. MICHAEL H. EBERT, DR. V. LEAF and (by invitation) DR. S. BARSKY.

A. P., a 31 year old Italian housewife, first noticed two small, firm "pimples" above the left eyebrow about three years ago.

She states that one of the lesions has become progressively larger; within the past year the larger lesion was cauterized and given X-ray treatments (quantity unknown).

She came to this country from Italy about six months ago. For the past three months she has worked in a factory as a television assembler. No history of trauma or exposure to beryllium was obtained. The patient has always been in good general health and states that no member of her family has ever had tuberculosis.

Physical examination reveals an essentially normal condition except for a 1 by 1 cm. reddish pink, nontender, firm, nonfixed mass with soft center located immediately above the inner aspect of the left eyebrow. Two small, pea-sized lesions of similar appearance and consistency are situated in the immediate vicinity of the larger lesion. No lymphadenopathy or hepatosplenomegaly is noted.

Laboratory examination revealed the following results: urine, normal; hemoglobin, 87 per cent; white blood cells, 8,500, with normal differential count; sedimentation rate, 22 mm.; hematocrit volume, 41 per cent; Kahn reaction (blood), negative; total protein, 6.4 Gm. (albumin-globulin ratio, 4.4 : 2.0); roentgenogram of chest, normal; roentgenogram of long bones, normal; Mantoux test reaction (1 : 10,000), 2+. Biopsy was made of the large lesion on the forehead.

DISCUSSION

DR. J. E. GINSBERG: At the last meeting Dr. Oliver and those of us of his own staff at Hines showed a case in a relatively young man who had a number of lesions on the right side of the face—soft, papular lesions—and the case was presented as sarcoid(?). Dr. Caro and Dr. Rostenberg suggested examination of the sections of the lesion microscopically with polarized light. That was done, and we did find doubly refractile crystals, mostly amorphous, which were probably silicon. A number of similar cases have been reported in the British literature. In the *British Journal of Dermatology and Syphilis* for March 1950 Summerville reports a case of pseudotuberculoma silicoticum. Some of these lesions have developed as much as 29 years after small silicon particles were rubbed into the skin.

I think these tumors in Dr. Ebert's case resemble somewhat the small tumors in the case we showed last month. I think the microscopic section should be examined with the polarized light to see whether silicon can be found. The microscopic sections as I saw them today do not resemble those described in the literature or those presented by Dr. Oliver at the last meeting, in which the reaction shown was primarily a foreign body or giant cell reaction. There were numerous giant cells. In Dr. Ebert's case today the structure is that of a typical Boeck's sarcoid, but I think the sections should be examined under polarized light.

DR. ADOLPH ROSTENBERG JR.: I should like to mention the case referred to that is called pseudotuberculoma silicoticum (*Brit. J. Dermat.* **62**:105 [March] 1950). Recently I read an article dealing with the development of silicon reactions in the lungs of patients exposed to silicon. The author suggested, and had some experimental evidence, that the lesions actually arise because of what is known as a piezoelectrical effect. When pressure is brought on certain crystals an electric current is set up. Silicon is one of the materials in which that action occurs (Evans, S. M.: Tissue Responses to Physical Forces: I. The Pathogenesis of Silicosis, *J. Indust. Hyg. & Toxicol.* **30**:353 [Nov.]1948; II. The Response of Connective Tissue to

Piezoelectrically Active Crystals, ibid. **34**:592 [May] 1949). With expiration and inspiration, pressure on the lung tissue is exerted and there is evidence that an electrical current can be generated.

In the case that was presented last month one of the objections to the diagnosis of silicon reaction was that the sand blast injury occurred more or less equally over the face, neck and anterior chest wall but the lesions were only on the face and side of the neck. I think the piezoelectrical effect explains this observation, as the involved areas are areas of motility as compared with the uninvolved ones. If there is anything to this phenomenon one would get an electrical effect in the areas of greater motility rather than in areas of relative quiet, as the chest.

I think we should distinguish between the terms sarcoid and sarcoidosis. I do not think I am being pedantic. There is quite a difference: one condition is a morphological reaction, and the other is a complicated entity with definite characteristics. I have been looking over some of the literature in relation to sarcoidosis, and there are gradually being included a variety of conditions under this general label. I do not know whether that fact is good or bad. In one sense it is bad because we have no fixed idea of the etiology or pathogenesis of sarcoidosis. Unless we confine that label to a group of cases with relatively strict criteria, we will have heterogeneous cases under a label for disorders of which we do not know the cause and we will be in greater difficulty in determining the etiology. I think that the term sarcoidosis should be employed when there are certain specific systemic manifestations as well as skin manifestations and that if there are only skin lesions we should speak of a sarcoid reaction.

Lupus Vulgaris Erythematosus. Presented by Dr. Clark W. Finnerud, Dr. Frederick J. Szymanski and (by invitation) Dr. C. Glen Haner.

Multiple Benign Cystic Epithelioma. Presented by Dr. David Cohen and Dr. Theodore Cornbleet.

Poikilodermatomyositis with Lupus Erythematosus-Like Changes Associated with Calcinosis Cutis in a Twenty-Three Year Old Woman. Presented by Dr. A. H. Slepyan and (by invitation) Commander William N. New (MC), U. S. N.

A Case for Diagnosis: Xeroderma Pigmentosum, Abortive Form? Presented by Dr. Stephen Rothman and (by invitation) Dr. Sidney Steinberg and Dr. Calvin J. Dillaha.

Purpura. Presented by Dr. F. E. Senear and Staff.

A Case for Diagnosis: Circumoral Erythema. Presented by Dr. E. M. Smith Jr.

Lupus Erythematosus (Vesicular?). Presented by Dr. Harold Shellow.

Multiple Hemangiomas. Presented by Dr. Stephen Rothman and (by invitation) Dr. Fred V. Hauser.

Subepidermal Fibrosis, Probably Histiocytoma. Presented by Dr. Michael H. Ebert and (by invitation) Dr. Harold M. Spinka.

Erythema Multiforme Bullosum? Presented by Dr. F. E. Senear and Staff.

Plummer-Vinson Syndrome in a Twenty-Seven Year Old Woman with Disease of the Colon. Presented by Dr. H. Rattner, Dr. H. Rodin and (by invitation) Dr. D. Musgrave.

Sarcoid-Like Tuberculosis of the Skin. Presented by Dr. James R. Webster, Dr. S. M. Bluefarb and (by invitation) Dr. D. Musgrave.

Papulonecrotic Tuberculid Associated with Erythema Induratum. Presented by Dr. H. Rattner, Dr. H. Rodin and (by invitation) Dr. S. Barsky.

Superficial Epitheliomatosis. Presented by Dr. Michael H. Ebert, Dr. V. Leaf and (by invitation) Dr. D. Musgrave.

Dermatomyositis. Presented by Dr. Theodore Cornbleet, Dr. D. Cohen and (by invitation) Dr. S. Barsky.

Acrosclerosis. Presented by Dr. Theodore Cornbleet and (by invitation) Dr. H. Schorr and Dr. D. Musgrave.

Dermatofibrosarcoma. Presented by Dr. D. Omens and (by invitation) Dr. H. Omens and Dr. D. Musgrave.

Sclerosing Hemangioma. Presented by Dr. Michael H. Ebert and (by invitation) Dr. A. Pearl and Dr. S. Barsky.

Theodore Cornbleet, M.D., *President*

James R. Webster, M.D., *Secretary*

Oct. 18, 1950

Circumscribed Scleroderma ("Linear"? "Zosteriform"?). Presented by Dr. Julius E. Ginsberg.

Linear Scleroderma with Extreme Atrophy of Lower Limb. Presented by Dr. Stephen Rothman and (by invitation) Dr. Douglas N. Buchanan.

DISCUSSION

Dr. Paul A. O'Leary, Rochester, Minn.: A diagnosis of circumscribed or linear scleroderma seemed warranted for Dr. Ginsberg's patient, and Dr. Rothman's case was also one

of scleroderma of the hemiatrophic type. The unusual feature in the second case was the pronounced atrophy—cutaneous, muscle, and bone—limited to the right leg, with no evidence of cutaneous sclerosis of the arm or face. Scleroderma of the scalp and forehead, the encoup de sabre type of lesion, frequently precedes the appearance of a similar process in the arm and/or leg.

Both of these cases emphasize the point that these cutaneous lesions are probably of central nervous system origin, the skin lesions being trophic disturbances—if I may use that term loosely—as the result of trauma to the brain stem, either actual or from an infectious agent. Rubin, and also Wartenberg, have called attention to the nervous system relationship of these conditions.

Specific treatment is not available. Bismuth therapy may help the morpheic forms of the disease, and the local application of heat and massage will do the same. Morphea is a self-limited disease, in my experience, requiring six to eight years to involute. Sympathectomy did not prevent the development of the hemiatrophy when done in early cases, nor were the children improved who had pronounced atrophy at the time of operation. Cortisone has produced a rapid involution of the scleroses in patients with the early types of acrosclerosis, and most of them maintain the skin softening of the fingers for several months before the sclerosis returns; however, small maintenance doses have not kept the skin soft.

Dr. Louis Rubin, Rockford (by invitation): The child Dr. Rothman and Dr. Buchanan presented today is one of the children included in the series I reported (Arch. Dermat. & Syph. **58**:1-18 [July] 1948). She was one of the children who showed a lack of fusion of the arches of the fourth lumbar vertebra. At that time, however, she was at the age (5 or 6 years) when fusion is not always complete. She also had involvement of the buttock on the same side as the leg involvement. There has been considerable progression since that time. I believe more of these cases should be investigated from a neurologic viewpoint so that we might arrive at a more definite conclusion as to the role of the nervous system in this condition.

A Case for Diagnosis: Pemphigus Vegetans? Pyoderma Vegetans? Presented by Dr. Stephen Rothman and (by invitation) Dr. E. Farney-Davies.

DISCUSSION

Dr. Louis A. Brunsting, Rochester, Minn.: In this case, of an elderly woman with a vesicular reaction of serpiginous configuration limited to the region of the vulva, I prefer to use the term "dermatitis vegetans" or "pyoderma vegetans" rather than to bring in the term "pemphigus," because of its vicious connotation. Sometimes such an eruption is a reaction of sensitivity; Underwood and I have reported several instances of this type of lesion in patients who had chronic ulcerative colitis. In one patient the eruption recurred each time one of the sulfonamide drugs was administered. In such a case there is a high percentage of eosinophils in the tissues locally and in the circulating blood. The course of the disease is chronic and recurrent, but the disorder is not a part of pemphigus vulgaris. In my opinion, such infectious elements as may be identified by culture usually are secondary invaders.

A Possible Case of Hodgkin's Disease with Severe Pruritus and Multiple Excoriations. Presented by Dr. Herbert Rattner, Dr. Harold Rodin and (by invitation) Dr. J. F. Sickley.

Mycosis Fungoides. Presented by Dr. Herbert Rattner, Dr. Harold Rodin, and (by invitation) Dr. Stefan Bielinski.

Myelogenous Leukemia with Specific Purpuric Lesions of Myelogenous Leukemia. Presented by Dr. James Webster, Dr. Samuel Bluefarb, and (by invitation) Dr. Stefan Bielinski.

Lymphoma Cutis. Presented by Dr. Paul P. Boswell.

Leukemia Cutis? Presented by Dr. Matthew Block (by invitation) and Dr. Stephen Rothman.

DISCUSSION OF PRECEDING FIVE CASES

DR. STEPHAN EPSTEIN, Marshfield, Wis.: I should like to discuss Dr. Boswell's case. There was a particularly striking picture, with a reticular and linear pattern, especially on the shoulders, the neck, and the axillas. It looked as though it should be some entity. I am not sure I know what it is, but I believe the picture belongs to a certain form of lymphocytoma. The histologic picture fits in well with lymphocytoma. There is an infiltrate of lymphocytes which is a little less cellular than that usually seen in lymphocytoma. Ordinarily lymphocytomas consist of single or multiple tumor-like lesions or of grouped miliary nodules. However, there is also a particular form of more generalized "miliary lymphocytomas." Some 20 years ago Mulzer and Keining (*Dermat. Wchnschr.* **1**:293, 1929) described such a case, of a more widespread linear eruption, which resembles this one very much. Berde and Lang (*Dermat. Wchnschr.* **1**:641, 1935) reported a similar case. I observed a similar case (*Arch. Dermat. u. Syph.* **173**:188, 1935) but never published it because I hoped I would see another one. I believe the case presented belongs to this group. Neither Mulzer and Keining's nor our own case turned into leukemia.

Dr. Michelson reminded me that Bäfverstedt (*Acta dermat-venereol.* (supp. 11) **24**:1-202, 1943) had recommended penicillin for the treatment of lymphocytoma. I believe a trial of penicillin therapy might be interesting in this case.

DR. MATTHEW BLOCK: Cases of atypical leukemia present quite a difficult diagnostic problem. Our patient had typical lymphatic leukemia in 1939 with a white cell count of 90,000, with 95% lymphocytes. Biopsy of a node at that time revealed giant follicular lymphoma. Now the peripheral blood is perfectly normal, as is the marrow, as proved by surgical biopsy of the sternal marrow. Recent biopsy of a lymph node revealed giant follicular lymphoma. A section from the liver was characteristic for lymphatic leukemia.

The point I would like to make is that in these patients with lymphomatous skin lesions and normal peripheral blood, if you look far enough, in the spleen, liver, marrow, or lymph nodes some other evidence of the lymphoma will be found. It is also possible that the patient may have more than one variety of lymphoma at the same time.

Acne Following ACTH Therapy for Arthritis. Presented by DR. M. J. BRUNNER.

The patient, a 24-year-old woman, was placed on a high-protein, high-caloric diet, and treatment with ACTH (Wilson), 20 mg. three times daily by intramuscular injection, was started. After 22 days, a salt-free diet was given because of the development of edema. After 28 days the dose of ACTH was reduced to 10 mg. three times daily, and, after 35 days, to 5 mg. three times daily. The patient was discharged on this schedule on July 25, 1950.

Improvement in joint manifestations was noted after 24 hours on ACTH therapy. After two weeks of therapy, a Cushing syndrome developed, with fluid retention, hypertension (blood pressure of 154/100), acne of the face, upper arms, and back, a moon-shaped face, and increased pigmentation of freckles. The absolute eosinophil counts were 170 before administration of ACTH and remained near 0 during therapy.

The urinary 17-ketosteroids increased from 8 mg. per 24 hours on the first day to 14.5 mg. on the second day and 21.5 mg. on the third day and remained at high levels throughout the period of treatment, finally reaching 82.5 mg. on the twenty-seventh day. Biopsy specimens from the thigh were taken before and during ACTH therapy.

The patient was seen in the Dermatology Clinic of the University of Illinois on Aug. 11, 1950, because of the persistence of her acne. At that time there were numerous small, red-brown papules and some comedones and pustules diffusely scattered over the face, shoulders, upper arms, and back, examination of which revealed inspissated sebum filling the follicular orifices. There was no significant inflammatory reaction.

Diffuse, Dry Neurodermatitis Treated with ACTH. Presented by DR. STEPHEN ROTHMAN and (by invitation) DR. E. FARNEY-DAVIES.

W. B., a 30-year-old white man, was first seen at the University of Chicago Clinics in October, 1949, with a history of "eczema" since the age of 3 months. During early childhood the eruption was limited largely to flexural areas, but from the age of 15 years it has tended to become generalized.

At the age of 8 years the patient manifested seasonal hay fever, which subsided greatly at the time the eruption became more generalized. In 1944 he had "eczema vaccinatum" following smallpox vaccination.

During the past year the eruption has been extensive, extremely pruritic, and incapacitating. The patient's response to therapy during two long periods of hospitalization has been slow, with immediate exacerbation on discharge, even when he moved to the Southwest.

On Oct. 5, 1950, he was readmitted to Albert Merritt Billings Hospital for ACTH therapy. Within 24 hours after the initiation of treatment (100 mg. per day in divided doses) he experienced dramatic relief from itching, and since the third day of treatment he has had no itching. Within 36 hours all weeping had subsided and there was decided blanching of the skin. After 10 days no change in the lichenification, most prominent on face, neck, large flexures, and wrists, is apparent.

The patient feels well and is relaxed, his only complaints being that he has some difficulty sleeping and continues to have at least one episode of profuse diaphoresis daily. At present he is receiving 80 mg. of ACTH every 24 hours in divided doses. A biopsy specimen taken before ACTH therapy is presented.

Pemphigus Treated with Cortisone, ACTH and Testosterone Propionate. Presented by Dr. Frederick R. Schmidt.

The patient, a 57-year-old man, has been treated with 2.2 gm. of cortisone, 7 gm. of ACTH and 300 mg. of testosterone propionate. Twelve grains of potassium chloride were given daily. A salt-free diet has been maintained throughout. A daily dose of 100 mg. of ACTH in conjunction with biweekly injections of 25 mg. of testosterone propionate was found necessary to maintain the patient in his present state.

Psoriasis Vulgaris Treated with ACTH. Presented by Dr. Alfred B. Falk and (by invitation) Dr. Francis Hetreed.

K. G., aged 3 years, was well until April 1950, when she manifested a rash on her face and scalp, which became generalized in a few weeks. Treatment on an outpatient status was unsatisfactory, and so the patient was hospitalized. There was no response to local treatment.

Treatment consisted in autohemotherapy, 10 cc. three times a week for eight injections. Since there was no improvement, ACTH therapy was started. The patient received 10 mg. four times a day for 18 days. The eosinophil count was 181.25 at the start and 56 two days later; it then stayed between 31 to 43 cells per cubic millimeter.

The response to the administration of ACTH was rapid. Redness subsided appreciably in three days. However, at no time was the skin clear of lesions. At the termination of therapy much scalp hair began to shed spontaneously.

Kodachrome® slides show the status of the patient before starting ACTH therapy and on ceasing therapy.

DISCUSSION OF PRECEDING FOUR CASES

Dr. Louis A. Brunsting, Rochester, Minn.: Today we have seen examples of a number of diseases of varied clinical and pathological patterns which respond in some measure to the administration of cortisone or ACTH. This does not imply that such diseases have a common etiologic factor. In most instances these hormones suppress the reactive phenomena such as fever, arthritis, and the elevated sedimentation rate, and they promote a sense of well-being and a gain in general health, but, with all this benefit, there is little permanent influence on the significant underlying disease. In the sick patient with disseminated lupus erythematosus, psoriasis with arthritis, and pemphigus vulgaris, these beneficial effects are variable, depending on the nature of the illness and the extent of the damage that has been done; the effects are also more or less temporary unless adequate dosage is maintained, in which event there may be unfavorable repercussions in other respects. As Hench has emphasized, these hormones are not curative. They provide a means of controlling the reactive symptoms in apparently unrelated diseases; they also provide a tool for the study of the physiologic processes in health and disease. At the present time, the range of their therapeutic application and the establishment of optimal schedules of dosage are being appraised. Any tendency to apply these hormones indiscriminately in treatment without appreciation of their potency is only to be condemned.

DR. JAMES H. MITCHELL: I reported last year on the treatment of two cases of mycosis fungoides. In one this eventuated into Hodgkin's disease. The patients were treated intensively with ACTH while at the hospital and after that with cortisone. Both acquired severe emotional disturbances. One had a terrific laughing attack. One later acquired severe and permanent diabetes. The medical staff members at the hospital have treated a number of patients with neurodermatitis and other conditions of like nature. The patients received only temporary benefit. They have had rather severe side reactions. Personally, I am through with ACTH. Last spring I reported the cases of two boys with lupus erythematosus acutus. They were benefited by ACTH therapy for the time being, but each has had exacerbations and recurrences as severe as any of the previous attacks.

Autopsy was performed in both cases of mycosis fungoides or lymphoblastoma, and there was no demonstrable change in the adrenals.

DR. THEODORE CORNBLEET: I should like to ask Dr. Brunner whether there were any comedones in his case.

DR. M. J. BRUNNER: When the patient was first seen she had a good many comedones interspersed in an acneform eruption. It was more extensive and acute than it is today. We were able to demonstrate the fact that some of the lesions were comedones by expressing them with a comedone extractor and having a white plug emerge. In addition, we made a biopsy of two lesions. One of the slides showed filling of the follicle orifice with what was apparently inspissated sebum. I think it is evident that there were present the usual comedones of acne.

Since seeing this case, Dr. Riddell, Dr. Rostenberg, and I have been collecting cases, on all the services at Illinois as well as at Presbyterian Hospital, in which ACTH, or cortisone, or both were given. We have accumulated 100 such cases. About 25 acquired acne, generally not as severe as that in the patient you saw today. Hers is the most widespread acne reaction we have seen. In addition to acne we have found, even more frequently, the development of hyperpigmentation, which may be generalized though sometimes is localized in the areas of previously present eruption or in moles. In two instances the pigmentation occurred on the buccal mucous membrane. In the records there was also mention of other side-effects pointed out by Dr. Brunsting—that is, Cushing's syndrome, hypertrichosis, and the development of striae on the abdomen.

DR. STEPHEN ROTHMAN: The advent of ACTH and cortisone has raised most difficult psychologic, social, and moral problems. If Dr. Mitchell says he is through with ACTH I wonder how can he withstand the pressure of the family of a patient who is moribund with pemphigus or disseminate lupus erythematosus. However, I fully agree that in recurrent, chronic, nonfatal diseases one should exert great restraint in using these drugs because of the early relapses and because the patient may become dependent on the drug. Repeated courses may ruin him somatically, pyschically, and financially.

Our presented patient with dry diffuse neurodermatitis responded dramatically in the first 48 hours and has been without any complaint ever since. His itching subsided promptly long before he could develop "euphoria." We have studied the problem as to whether local tar application acts on lichenified skin which does not itch. So far we have seen no effect of the local tar application under such circumstances. The treated and control sites showed no differences.

The papular acneform eruption which is seen in patients of all age groups under ACTH treatment is not identical with the picture of juvenile acne. Oleic seborrhea is not present, and in our experience comedones are seen only exceptionally. It seems that ACTH induces follicular hyperkeratosis, which is one factor in the development of juvenile acne, but it does not induce hyperplasia of sebaceous glands. This theory seems to be borne out by measurements of sebum excretion and by measurements of sebaceous gland cross sections before, during, and after ACTH treatment.

The hyperpigmentation of healed lesions in pemphigus has been quite conspicuous. The pigmentogenic action of ACTH may be connected with a decrease of glutathione in the skin.

Sarcoidosis of the Left Breast Region. Presented by DR. THEODORE CORNBLEET, DR. DAVID M. COHEN and (by invitation) DR. STEFAN BIELINSKI.

The patient is a 29-year-old Negro who manifested a lesion of the left breast area about one month prior to entry to the Cook County Hospital. The lesion began as small nodules,

which coalesced and infiltrated an area approximately 4 by 8 in. (10 by 20 cm.), extending to the midaxillary line. The only subjective complaint was mild itching of the involved area.

The temperature was 98.4. The lesion is a deeply infiltrated, purplish-red plaque covering the left breast area and extending laterally to the midaxillary line. There are discrete nodules at the periphery of the plaque, and the entire lesion is covered by coarse, dry scales. The lesion is not tender, and there is no definite attachment to the underlying structures. There is no regional adenopathy.

Biopsy of the skin revealed the picture of sarcoid.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: I have so often discussed the difference between making a diagnosis of sarcoidosis and making one of sarcoid reaction that I do not want to take up your time with that again.

In the case presented this afternoon, there was very little eruption although there was infiltration in the pectoral region. The patient had been using a strong ointment after an injury, and the resulting condition altered the picture considerably. The microscopic section also was not entirely acceptable to me, and so, all in all, I doubted the diagnosis.

(NOTE.—Dr. Caro later sent me another slide, and in that section the diagnosis of sarcoid was clearly established.)

DR. M. R. CARO: I am very happy to agree with Dr. Michelson, as I nearly always do, that there is no such thing as a diagnosis of sarcoidosis histologically. All one may say after examining a section is that there is a sarcoid reaction. A few weeks ago my associates and I saw a very beautiful sarcoid histologic picture which turned out to belong to a case of secondary syphilis. I well recall a section that I presented as a sarcoid a few years ago which also turned out to be from a case of secondary syphilis. I have also seen sarcoid reactions histologically in leprosy, tuberculosis, and beryllium granulomas.

All I can say for this particular section is that there are many sharply outlined nests of epithelioid cells with very few lymphocytes. In diagnosing this section as sarcoid I do not imply that the patient has sarcoidosis with lung or bone involvement. Before a diagnosis of sarcoidosis can be established a more complete examination should be done. I believe that in this case the diagnosis of sarcoid is acceptable clinically as well as from the section. The small discrete papules at the border were diagnostic, even though the large infiltrated mass was unusual. I should like to have a biopsy performed on a section from the infiltrated area beneath the breast. It may be that this mass represents a very diffuse type of sarcoid involvement.

A Case for Diagnosis: Livedo Reticularis (?) in a Twin. Presented by DR. STURE A. M. JOHNSON, Madison, Wis.

DISCUSSION

DR. M. H. EBERT: I thought this was an extremely interesting case; however, I doubt that my discussion will throw much light on the final diagnosis. According to the history the reticulation of the livedo in this case was more marked early in the course of the disease than it is at present. The reticulations of the livedo are due to the distribution of the deeper arteries in the skin. If there is a vasospasm in these arteries there will be stasis in the area supplied by the terminal filters from the main artery, giving this peculiar picture. Usually this vasospasm is preceded by cold. I considered the diagnosis of acrocyanosis. This is usually seen in fleshy young women, presenting the clinical picture of edema and bluish discoloration of the ankles with livedo of the legs. However, there was nothing to warrant such a diagnosis in this case. The livedo patterns may be the site of inflammation with tuberculosis or syphilis, in which case we have a clinical picture of livedo reticularis. The sections in this case seem to show that the basic lesion is a pronounced vasculitis. It is possible that this may be due to a hypersensitivity to some ingested drug. There is no evidence for this theory in the history. There does not seem to be enough change to call the condition periarteritis or panarteritis.

DR. STURE A. M. JOHNSON, Madison, Wis.: This patient has been exceedingly interesting to us because we made a diagnosis of livedo reticularis and for that reason started studies on the vascular system of the legs. Since the livedo reticularis was seasonal, being much worse in the summertime, we thought it might be an allergic condition. Drugs having sympathetic or

parasympathetic action were given without effect. Only tripelennamine (pyribenzamine®) has controlled the livedo and the accompanying dermatitis. Exacerbation of the process takes place when tripelennamine is withdrawn. A tuberculin test performed four years ago elicited negative reactions. The possibility of the livedo reticularis being a manifestation of periarteritis nodosa will be studied further.

Chronic Porphyria (Tardive Congenital). Presented by Dr. Stephen Rothman and (by invitation) Dr. Calvin J. Dillaha, Dr. Allan L. Lorincz, and Dr. Delbert Bergenstal.

A. C., a 48-year-old white woman, was first seen at the University of Chicago Clinics on Sept. 8, 1950, with a chief complaint of excessive hair growth on her face associated with a descent in the hair line of her forehead of three years' duration. About the same time she observed increased darkening of her face. Occasional pruritus of her face has been noted for the past year. In the past two months she has noted the appearance of bullae on her hands and fingers following mild trauma. Her urine has been dark for the past two years.

For more than 20 years the patient has indulged in two or three cocktails each evening before retiring.

Exophthalmos has been present 25 years, and 10 years ago a subtotal thyroidectomy was performed.

No family history of porphyria was elicited.

Laboratory Studies.—The urine was orange-red and fluoresced red under the Wood light; otherwise it was normal. The native urine on spectroscopic examination showed the characteristic bands of the free porphyrins. The test for porphobilinogen gave negative reactions.

A determination of the 24-hour urinary porphyrins revealed 6.7 mg. of uroporphyrin and 6.5 mg. of coproporphyrin. Separation of the coproporphyrin isomers is now in progress.

There was a mild hyperchromic anemia. The sedimentation rate was 45 mm. in one hour (uncorrected). Liver-function studies are now in progress.

DISCUSSION

Dr. Louis A. Brunsting, Rochester, Minn.: This woman presents the characteristic cutaneous signs of chronic porphyria. During the past three years she has noted a gradual change in complexion with a darkening of the exposed features and some bluish-red coloration of the cheeks and the upper part of the trunk. The scleras are injected, and there is hypertrichosis. Recently a blistering reaction on the fingers and forearms has appeared, but the relationship to exposure to sun is not definite. The skin is unusually susceptible to minor trauma. Abnormal porphyrins, particularly uroporphyrin, are found in the urine in large amounts.

In my experience, the ingestion of alcohol has been the most important factor in precipitating clinical symptoms in persons who have latent porphyria. In this case, the patient readily admits to the daily ingestion of alcoholic drinks, and I should guess that test will indicate an interference with normal liver function. The genetic pattern of porphyria is not clear. As more patients with porphyria are identified, the types of porphyrins classified and screening surveys made of families of such patients, we shall learn more about the genetic pattern. For the present, as regards treatment, there is no direct approach except to prohibit the use of alcohol and other hepatic toxins such as barbiturates and to institute dietary measures of control similar to those which are prescribed in hepatic cirrhosis.

Dr. Stephen Rothman: Dr. Kluever has demonstrated in animal experiments that porphyrins are selectively deposited in the pituitary glands. Possibly the hypertrichosis is due to pituitary stimulation which comes about by this deposition.

Erythroderma Exfoliativa (Secondary to Pityriasis Rubra Pilaris?) in a Nine-Year-Old Girl. Presented by Dr. Stephen Rothman and (by invitation) Dr. Lydia C. Marshak.

DISCUSSION

Dr. F. E. Senear: This patient, as the history indicates, was shown here before by Dr. Caro as having pityriasis rubra pilaris. That diagnosis was acceptable to everyone. I saw the child in June of this year, she having been free of lesions for several years during the

interim since Dr. Caro had seen her. When she first came to me she had an indisputable picture of pityriasis rubra pilaris. She had a great many follicular lesions, which lesions coalesced to form patches of erythrodermic type. The original attack followed an episode of middle-ear infection for which penicillin was used. The skin condition began immediately afterward. We saw her in June, and in July she acquired another infection, for which she was given aureomycin by mouth. Afterward she had universal erythema and for the first time the legs were involved. Thereafter the reaction subsided and follicular elements disappeared completely. At no time did I have any thought of this being a universal erythroderma following psoriasis as we so often see it.

Incidentally, the patient was seen by one of our colleagues, who made a diagnosis of lichen ruber acuminatus, the old name given by the Germans to pityriasis rubra pilaris. After treatment supposed to be useful in that condition, she was placed on arsenic therapy, and that apparently caused some exacerbation of the condition. With the vitamin A administered under Dr. Caro's care she was eventually cured. With vitamin A therapy this time in our hands she showed no improvement. The last time I saw her I suggested to the pediatrician that we might try thyroid in small doses, since Dr. Zeisler had tried that with success. Today she shows on the legs a very acute exacerbation which she did not have until after she had been given aureomycin.

DR. M. R. CARO: This afternoon I examined the section before I saw the patient and I made a histopathologic diagnosis of psoriasis. I was very much surprised when I saw the patient to recognize one that I have treated for two separate attacks of pityriasis rubra pilaris. Approximately three years ago (ARCH. DERMAT. & SYPH. **60**:867, 1949) I presented her before this Society very early in her first acute attack, which followed the administration of penicillin. The eruption cleared up gradually after the administration of 300,000 units daily of vitamin A by mouth, and she remained well for about three years. I saw her again early this year for a recurrent attack of classic pityriasis rubra pilaris, which again followed the administration of penicillin for some type of infection. The characteristic lesions have apparently spread to produce the picture that is present today. The interesting thing about this case is the onset of both attacks very soon after penicillin was administered.

I have under my care another patient of about the same age in whom also two attacks of pityriasis rubra pilaris followed the administration of penicillin for some infectious disease. I saw her soon after the onset of the eruption in both attacks, and both times the skin became normal after the administration of vitamin A by mouth. I wish you would all look for cases of pityriasis rubra pilaris following the use of penicillin.

DR. S. J. ZAKON: Apropos of this case, I would like to recall to you that vitamin A is not a harmless drug. Recently I saw a child who was brought into the hospital with acute fever and bone pain and intense itching, which was due to an excess of vitamin A. The child recovered, but X-ray study revealed some definite changes in the long bones.

DR. STEPHEN ROTHMAN: I did not doubt the correctness of the diagnosis of pityriasis rubra pilaris made by those who saw the child before the generalization. The question mark was meant to indicate that at present this diagnosis cannot be established. The child's condition has remarkably improved since she has been on treatment with moderate doses of vitamin A.

Erythema Multiforme-Like Eruption. Presented by DR. M. H. EBERT, DR. A. PEARL and (by invitation) DR. J. F. SICKLEY.

Psoriasis with Exfoliative Dermatitis? Presented by DR. M. H. EBERT, DR. V. LEAF, and (by invitation) DR. J. F. SICKLEY.

Paget's Disease of the Breast Unrecognized for Five Years, in an 80-Year-Old Woman. Presented by DR. DAVID OMENS, DR. HAROLD OMENS, and (by invitation) DR. J. F. SICKLEY.

Lichen Spinulosus in Siblings. Presented by DR. THEODORE CORNBLEET, DR. HENRY SCHORR, and (by invitation) DR. J. F. SICKLEY.

Calcinosis of the Fingers. Presented by DR. THEODORE CORNBLEET, DR. DAVID COHEN, and (by invitation) DR. STEFAN BIELINSKI.

Keratosis of the Palms Improved with Penicillin Injections. Presented by DR. THEODORE CORNBLEET, DR. HENRY SCHORR, and (by invitation) DR. STEFAN BIELINSKI.

Steatocystoma Multiplex. Presented by DR. A. W. STILLIANS.

Occupational Leukoderma from Rubber Products. Presented by DR. SAMUEL J. ZAKON and (by invitation) DR. AARON L. GOLDBERG.

Kaposi's Multiple Idiopathic Hemorrhagic Sarcoma: No Response to Treatment with Penicillin. Presented (by invitation) by DR. F. V. HAUSER and DR. A. L. LORINCZ.

Incontinentia Pigmenti? Systemic Nevus? Presented by DR. A. M. BUCHHOLZ.

A Case for Diagnosis: Lichen Sclerosus et Atrophicus of Genitalia in a Six-Year-Old Girl? Presented by DR. ALFRED B. FALK and (by invitation) DR. FRANCIS HETREED.

MANHATTAN DERMATOLOGICAL SOCIETY

Herman Sharlit, M.D., *President*

George M. Lewis, M.D., *Secretary*

May 9, 1950

Contact Dermatitis (Nickel). Presented by DR. JACK WOLF.

D. G., a woman aged 44, is presented from the New York Skin and Cancer Unit with an eruption on the hands, thighs and abdomen of three months' duration. In December, 1949, she acquired an eruption on the lobes of the ears which she attributed to earrings. When she stopped wearing them the eruption disappeared. In February, 1950, she manifested an eruption on her thighs and on the left side of the abdomen. In March an eruption appeared on the left palm. These areas have been getting progressively worse. The patient is a waitress and carries a metal tray at the site of the eruption on the left hand.

There is acute erythema, vesiculation, and scaling at all of the above-mentioned sites, which are areas which come into direct contact with metal: garters, the zipper on her girdle, and the tray. Patch tests were performed with nickel sulfate and a 5-cent piece. They gave strongly positive reactions.

Keratosis Pilaris; Ulerythema Ophryogenes. Presented by DR. JACK WOLF.

N. P., a man aged 23, is presented from the Skin and Cancer Unit of University Hospital with a generalized eruption which has been present since infancy. Both his father and his sister have a similar eruption, but in a milder form.

There is mottled erythema on the sides of the face, some telangiectasis, and a peculiar absence of hair in the bearded region. On the back of the neck, at the hairline and somewhat below, he presents a number of small match-head-sized keloidal lesions. The region of the eyebrows is erythematous, scaly, and hyperkeratotic, and some small atrophic spots are present; there is a diminution in the number of hairs. The greater part of the torso and extremities is covered with brownish, hyperkeratotic, pinhead-sized lesions at each follicular orifice. The pronounced pigmentation regularly distributed against the white background is most striking.

DISCUSSION

DR. ORLANDO CANIZARES: I was wondering whether the condition could not be some atypical form of Darier's disease.

DR. GEORGE C. ANDREWS: Some of these cases of keratosis pilaris are regarded as a follicular type of ichthyosis, and, since there is a family history of the disorder, it is probable that it is a mild ichthyotic eruption of the follicular type.

DR. JACK WOLF: The alopecia of the bearded region is typical of this disease. It occurs chiefly in women, so that one does not have the opportunity to demonstrate as well the effect of a long-standing follicular hyperkeratotic process which ultimately leads to atrophy. The question of whether the involvement of the bearded region, the eyebrows, and occasionally other parts is an extension of the keratosis pilaris, with which it is always found in association, or is a disease *sui generis* is not settled. I am inclined to the former opinion.

Poikiloderma Vasculare Atrophicans. Presented by DR. DAVID BLOOM.

DISCUSSION

DR. WILBERT SACHS: I think there may be some evidence now of mycosis fungoides.

DR. DAVID BLOOM: I don't know why we should make a diagnosis of mycosis fungoides. The condition may develop polymorphism, but all cases of poikiloderma show this pronounced infiltration.

Periadenitis Mucosa Necrotica Recurrens(?). Presented by DR. ORLANDO CANIZARES.
Linear Nevus. Presented by DR. NATHAN SOBEL.
Lichen Striatus. Presented by DR. DAVID BLOOM.
Infectious Eczematoid Dermatitis; Bronchiectasis. Presented by DR. ORLANDO CANIZARES.
Lichen-Planus-Like Drug Eruption(?). Presented by DR. ORLANDO CANIZARES.

LOS ANGELES DERMATOLOGICAL SOCIETY

Jud R. Scholtz, M.D., *President*

Molleurus Couperus, M.D., *Secretary*

May 9, 1950

Pemphigus Vegetans: Involution with Cortisone Therapy. Presented by DR. BEN A. NEWMAN and (by invitation) DR. FRED FELDMAN.

J. M. M., a man aged 49, had the beginning of the present illness in March 1949 with sores in the mouth and throat appearing in multiple groups. Treatment during the next several months was that for Vincent's infection and nonspecific infections of the mouth, although no definite evidence for this diagnosis was found on laboratory examination. Treatment consisted in the administration of penicillin, aureomycin, topical applications and vitamins. In August 1949, on examination by the presenter, the diagnosis of oral pemphigus was made. There were no cutaneous lesions at that time, and the observations on physical examination, blood count, results of urinalysis and sedimentation rate were all normal. The patient was given a second course of aureomycin without improvement, and he discontinued therapy for the next two months. In November 1949 he reappeared at the office with extensive involvement in the mouth, consisting of small blebs and superficial erosions, and blebs in the crural and intergluteal folds. Each of the crural blebs on rupturing developed small granulomas, which became confluent, so that in a period of eight weeks the patient manifested large cauliflower granulomatous masses involving the crural and inguinal folds, the perineum and the intergluteal folds.

During this period he lost about 15 pounds (7 Kg.) in weight. Therapy at this time consisted in several blood transfusions, 250 cc. each, and the administration of acetarsone, 0.25 Gm. three times daily, at three day intervals. Under this regimen, the mouth lesions were considerably improved but the vegetating lesions were unaffected and continued to increase in size with surface exudation and fissuring. In December the patient manifested an arsenical erythema. Medication was discontinued, and the mouth lesions became severer. One month later the man was again given smaller doses of acetarsone, which he was able to tolerate and which reduced the intensity of the mouth lesions.

In April 1950 the patient had been bedridden for three months because of the vegetating lesions of the groin, weakness and loss of weight. On April 12 cortisone therapy was started. He received 100 mg. every second day for five doses and 25 mg. doses during the last 10 days as withdrawal doses, for a total of 775 mg. The last dose was given on May 5, 1950. In one week, all the vegetations had completely flattened and the skin presented smooth, dry, erythematous plaques at the sites of the former lesions. These erythematous plaques have been gradually fading to a more normal color. The mouth and lip lesions also have completely healed, but there has been one new bleb in the mouth. The patient has gained more than 15 pounds in weight and states that he has felt better than at any time during the past 15 months. He also volunteers the information that on April 20, 1950, he was able to use a toothbrush for the first time since the onset of his illness.

Biopsy of a vegetating lesion showed a picture typical of pemphigus vegetans.

DISCUSSION

DR. LOUIS H. WINER: The effect of cortisone on the vegetating lesions in this patient was dramatic. The action of cortisone, which tends to reduce eosinophilia, is a good reason for its use here, since pemphigus vegetans contains intraepidermal abscesses consisting practically solely of eosinophils.

A Case for Diagnosis: Psoriasis Vulgaris? Presented by DR. LOUIS H. WINER.

A Case for Diagnosis: Herpes Multiplex? Presented by DR. SAMUEL AYRES JR. and DR. SAMUEL AYRES III.

A Case for Diagnosis: Dermatitis Venenata? Presented by DR. JUD R. SCHOLTZ and (by invitation) DR. E. EARL KINZER.

Hemangiomatosis: Presented for Suggestions As to Etiology. Presented by DR. SAMUEL AYRES JR. and DR. SAMUEL AYRES III.

A Case for Diagnosis: Arsenical Keratoses with Epithelioma? Presented by DR. GORDON MACDONALD.

Behcet's Triple Symptom Complex. Presented (by invitation) by DR. RALPH B. COOMBER.

Pityriasis Rubra Pilaris. Presented by DR. SAMUEL AYRES JR. and DR. SAMUEL AYRES III.

Nevus Pigmentosus (Junction Type): Presented for Therapeutic Suggestions. Presented by DR. SAMUEL AYRES JR. and DR. SAMUEL AYRES III.

Dermatitis Artefacta with Scarring Resembling Lupus Vulgaris. Presented by DR. JUD R SCHLOTZ and (by invitation) DR. CRAIG WILLIAMSON.

Hemorrhagic Sarcoma of Kaposi. Presented by DR. PAUL D. FOSTER.

Boeck's Sarcoid (Sarcoidosis). Presented by DR. PAUL D. FOSTER.

Solid Edema of the Face (Pusey); Elephantiasis Nostras (Elliott); Recurrent Erysipelatoid (Fox). Presented by DR. J. WALTER WILSON.

Hodgkin's Disease. Presented by DR. JOHN D. ROGERS.

Obituaries

HENRY HONEYMAN HAZEN, M.D.
1879-1951

American Dermatology, and the Baltimore-Washington group of dermatologists in particular, lost a distinguished member when Henry Honeyman Hazen died on May 1, 1951.

He was born July 21, 1879, in Oldwick, N. J., the son of Dr. Davis H. Hazen and Emma L. Hazen (nee Honeyman). On both sides of his parents' families there had been many physicians, and this fact undoubtedly shaped the future of his life. He married Laura Mae Ross in 1908, and after her death he married Anita Burt, in 1922. He is survived by his widow and his son, Henry Honeyman Hazen Jr.

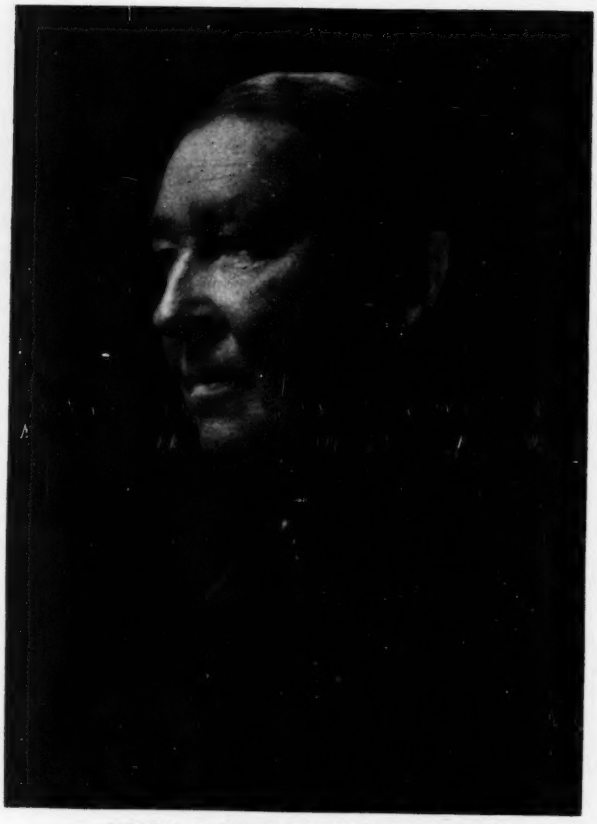
He was graduated from Central High School in 1898 and received his bachelor of arts degree from Johns Hopkins University when he was graduated in June, 1902. In 1906, he received his degree of doctor of medicine from the medical school of the same university. He interned at the Good Samaritan Hospital from 1906 to 1907 and at Saint Agnes Hospital from 1907 to 1908. After finishing his internship he became assistant in dermatology under Drs. Gilchrist and Lord at the Johns Hopkins Hospital.

In 1911, he was made professor of dermatology and syphilology at Howard University Medical School and remained in this position until 1944. Two years after he joined the faculty of Howard University Medical School he became professor of dermatology and syphilology at Georgetown University School of Medicine and taught in both schools concurrently. He resigned from the latter school in 1934.

He was active and held many important positions in the field of dermatology and syphilis, as follows: special consultant, United States Public Health Service, from 1918 to 1949; special consultant to the District of Columbia Health Department from 1942 to 1945; chairman of the National Prophylactic Committee, American Social Hygiene Association and the United States Public Health Service; chairman of the Advisory Committee of Public Education for the Prevention of Venereal Diseases for the United States Public Health Service from 1942 to his death; member of the National Advisory Serology Council, United States Public Health Service; secretary of the Section on Dermatology, American Medical Association, 1915 to 1918—chairman, 1919; president of the Social Hygiene Society of the District of Columbia, 1937 to 1945, and consultant dermatologist at Georgetown University Hospital, Freedmen's Hospital, Gallinger Hospital, and Columbia Hospital. He was certified by the American Board of Dermatology in 1933.

In 1925 he was given the honorary degree of master of arts by Georgetown University. He was a member of the American Medical Association, American Dermatological Association, Baltimore-Washington Dermatological Society, Southern Medical Association, and the Academy of Medicine, Washington, D. C., and a corresponding member of the Swedish Dermatological Association.

He published more than 170 papers on dermatology and syphilis and the following books: Diseases of the Skin, three editions, 1915 to 1927; Cancer of the



HENRY HONEYMAN HAZEN, M.D.
1879-1951

Skin, 1916; Syphilis, two editions, 1919 and 1928; Cutaneous X-Ray and Radium Therapy, 1931, and Syphilis in the Negro, 1942.

His hobbies were diverse; he was especially proud of his garden in Maine and of color photography as related to flowers but probably took a deeper interest in Oriental rugs, working on a manuscript on this subject up to within a few weeks of his death.

I cannot write this account in an altogether impersonal manner. I met Henry Hazen in the Skin Department of the Johns Hopkins Hospital in 1910, and for over 40 years we were close friends and dermatologic confreres. He was a fine, kind man, true to his specialty and profession and an indefatigable worker. In spite of his long-standing physical infirmities, he came to the local dermatologic meetings until he was incapacitated. He spent the last sixteen months of his life in pain and yet did not complain. His was a true courage.

HARRY M. ROBINSON

A. BENSON CANNON, M.D.
1888-1950

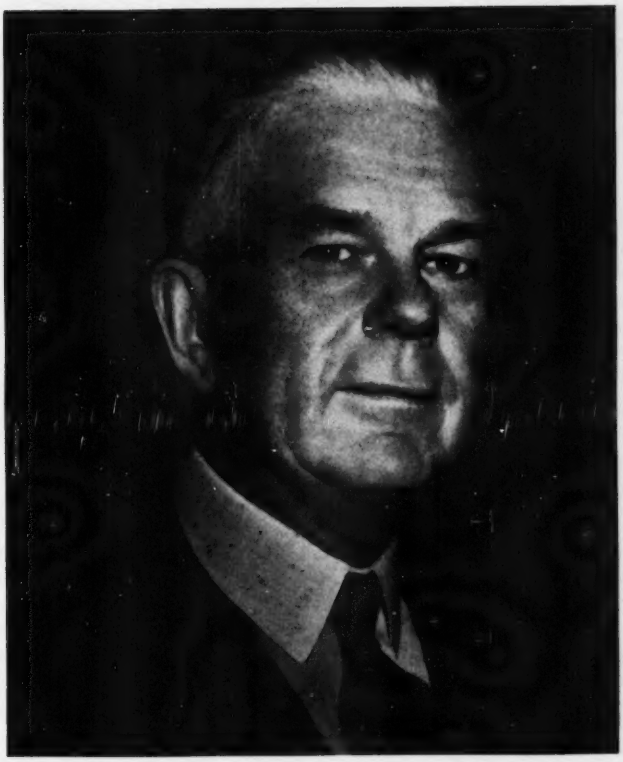
On Nov. 27, 1950, amid the surroundings he would surely have chosen, death came to Dr. A. Benson Cannon. He had been riding to hounds near his home in Millbrook, N. Y., that Thanksgiving week end, and had apparently dismounted to lower some bars, for there was no sign of a fall and his horse was standing quietly nearby. Happily, he never had to suffer what to him would have been the humiliation of failing powers, the incapacity of illness, the distress of those close to him. But for these persons the shock was inconceivable. He had epitomized bounding health and possessed a vigor of mind and body which belied his 62 years. Only the autopsy report of acute myocarditis explained his sudden death.

Dr. Cannon, son of Mr. and Mrs. Edmund Cannon, was born on Nov. 10, 1888, in Wilcox County, Alabama. He attended Erskine College in South Carolina and later became one of its trustees and recipient of an honorary doctor of laws degree. In 1909 he entered the medical department of Vanderbilt University, and the following year he transferred to Tulane, where he was awarded the degree of doctor of medicine in 1913.

Once possessed of a medical degree, Dr. Cannon turned to New York City. He had intended to become a gynecologist, but frequent contacts with Dr. John A. Fordyce and Dr. Homer F. Swift aroused his interest in dermatology. In 1916 he joined the staff of the College of Physicians and Surgeons of Columbia University and of the Vanderbilt Clinic as clinical assistant, and two years later he was appointed assistant attending dermatologist at City Hospital. These associations lasted until his death, at which time he was director of dermatology in both institutions, as well as Presbyterian Hospital.

Dr. Cannon spent much of the years 1924 to 1925 abroad, visiting dermatologic centers in England, Scotland, Germany, and France. He spent some time in Vienna studying at the Allgemeine Krankenhaus under Kyrle, Krenn, Oppenheim, Gertsman, and Kumer and there formed a lasting friendship with Leopold Arzt. On his return he opened his own office and equipped it with clinical and serological laboratories.

He had caught Fordyce's enthusiasm for syphilology, and he practiced and wrote widely in that field. With the advent of penicillin therapy, he obtained a special ward in Presbyterian Hospital and pioneered in the administration of that antibiotic in syphilis, maintaining a close relation with Dr. John F. Mahoney. With his accession to the professorship, he raised funds to establish and equip a modern serology laboratory within the department, and there quantitative tests became available for the first time at the Medical Center. He personally equipped a laboratory to conduct the treponemal-immobilization technic which has now become well established in the laboratory of the department, and at this writing nearly 300 tests have been run. Research in syphilology as a whole was a continuing project on which he worked



A. BENSON CANNON, M.D.
1888-1950

with groups of younger staff members and graduate students to establish the most effective treatment schedules in the various stages and manifestations of the disease, and reports on the subject are even now in press.

Syphilis by no means encompassed Dr. Cannon's special medical interests. In 1927 he published in the ARCHIVES a report on the treatment of 100 cases of chronic varicose ulcers from the wards of City Hospital by injection with sclerosing solution, in combination with pressure bandages. This was the first successful technic for sclerosing varicose veins to be introduced in this country, and it rapidly became established practice.

Lupus erythematosus was another disease in which he found particular challenge, and cutaneous cancer and its precursor lesions were always major concerns to him. His motion picture on "The Management of Cancerous and Precancerous Lesions of the Skin" was completed the week of his death and was shown posthumously at a meeting of the American Academy of Dermatology 10 days later.

His main interest, however, was always the individual patient. His real joy was in solving a diagnostic puzzle and, still more, in curing a desperate case.

Dr. Cannon gave great concern to the teaching functions of his department. Soon after assuming the professorship in 1947, Dr. Cannon formed an affiliation with the United States Marine Hospital at Stapleton, Staten Island. By that arrangement a well-equipped service of 65 dermatologic beds, in addition to wards for venereal disease, became available for teaching, and the residents at Marine Hospital were enabled to obtain basic training at the College of Physicians and Surgeons and to receive clinical instruction on their own wards by members of Dr. Cannon's staff accredited by the American Board of Dermatology and Syphilology.

He was equally interested in the teaching of undergraduates.

Dr. Cannon had little regard for the "ivory-tower" dermatologist. Nomenclature was for him only a means to an end. He was never able to convey by written word what was transmitted so easily by his personal magnetism and his devotion to the clinical challenge of which he never tired and on which his point of view never grew stereotyped or stale. He relied on his own experience and extraordinarily developed powers of observation, and so he taught his students. He consistently taught and practiced the belief that dermatology was an indispensable part of general medicine and that sound knowledge of general medicine, with a fair sprinkling from all the specialties, was essential to the proper practice of dermatology.

Outside of his profession, Dr. Cannon's great delight was horses and riding. He had a farm at Millbrook, N. Y., where he bred and trained horses, and he was an ardent member of the Millbrook Hunt and several others.

Those with the perception to penetrate his imposing but deceptive exterior found a remarkably shy, diffident person, sensitive, unable to bridge the gulf that separates man from man except where a span of intuition was stretched. Those truly close to Benson Cannon were extremely few, but with them an extraordinary devotion existed.

During his time abroad, Dr. Cannon had been struck by the number and size of the institutions devoted exclusively to dermatology throughout continental Europe

and the British Isles, and the conviction became deeply rooted in him that until comparable facilities were available in this country for bed patients, for clinical and basic investigative work, and therefore for teaching, dermatology would never achieve its maximum rate of growth. He devoted an increasing amount of thought and work toward this end in later years, and at the time of his death definite plans were under way. Those closely associated with him feel that he would almost certainly have succeeded and that in the untimely death of Benson Cannon dermatology lost not only one of its outstanding practitioners but also a man of vision who might in a few years have changed for the better the course of our specialty in this country.

Dr. Cannon is survived by his widow, the former Eleanor Reid, of Gastonia, N. C., and by his daughter, Cynthia.

J. LOWRY MILLER

Directory of Dermatologic Societies *

FOREIGN

Canadian Dermatological Association

E. Gaumond, President, 34 rue de la Fabrique, Quebec.
S. E. Grimes, Secretary, 404 Medical Arts Bldg., Ottawa.
Place: Seigniory Club, Montebello, Quebec.

German Society of Dermatology

Alfred Marchionini, Chairman, Dermatological Clinic, University of München.
Otto Grütz, Secretary, Dermatological Clinic, University of Bonn.

New Zealand Dermatological Society

P. E. Allison, President, 137 Cambridge Tce., "Harley," Christchurch.
R. G. Park, Secretary, Kelvin Chambers, 16 The Terrace, Wellington, C. I.

N. S. W. Branch of British Association of Dermatology and Syphilology

F. C. Florance, President, 135 Macquarie St., Sydney.
A. Geoffrey Finley, Secretary, 149 Macquarie St., Sydney.
Place: Royal Prince Alfred Hospital, St. Vincent's Hospital, Royal North Shore Hospital, Lewisham Hospital, Royal Alexandra Hospital for Children, and Newcastle Hospital, in rotation. Time: 4:00 p. m., on Fridays, approximately every two months.

North British Dermatological Society

President: Senior dermatologist in city where meeting is held.
A. Girdwood Fergusson, Secretary, 3 Ashton Rd., Glasgow, W. 2.

Royal Society of Medicine, Section of Dermatology

W. N. Goldsmith, President, 6 Upper Wimpole St., London, W. 1.
H. J. Wallace and D. I. Williams, Secretaries, 1 Wimpole St., London, W. 1.
Place: Royal Society of Medicine, 1 Wimpole St., London, W. 1. Time: 4:00 p. m., third Thursday of each month.

Sociedade Brasileira de Dermatologia e Sifilografia

F. E. Rabelo, President.
A. Padilha Gonçalves, Secretary, Caixa postal 389, Rio de Janeiro.
Place: Rio de Janeiro. Time: Last Wednesday of each month.

Sociedad Mexicana de Dermatologia

Silvestre Rico, Chairman.
Fernando Latapi, Secretary, Zacatecas 220-6, México, D. F.
Place: National School of Medicine, México, D. F. Time: 9:00 p. m., first Thursday of each month.

NATIONAL

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

Francis W. Lynch, Chairman, 1466 Lowry Medical Arts Bldg., St. Paul.
John H. Lamb, Secretary, 117 N. Broadway, Oklahoma City.
Place: Chicago. Time: June, 1952.

American Academy of Dermatology and Syphilology

Donald M. Pillsbury, President, 133 S. 36th St., Philadelphia 4.
John E. Rauschkolb, Secretary, P. O. Box 6565, Cleveland 1.
Place: Palmer House, Chicago. Time: Dec. 8-13, 1951.

American Board of Dermatology and Syphilology

Anthony Cipollaro, President, 40 E. 61st St., New York 21.
George M. Lewis, Secretary, 66 E. 66th St., New York 21.

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*Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date. The directory will be published in each July and January issue.

American Dermatological Association

Edward A. Oliver, President, 55 E. Washington St., Chicago 2.
Louis A. Brunsting, Secretary, 102 Second Ave. S.W., Rochester, Minn.
Place: Broadmoor, Colorado Springs, Colo. Time: April 23-26, 1952.

Society for Investigative Dermatology

Samuel M. Peck, President, 33 E. 70th St., New York 21.
Herman Beerman, Secretary, 255 S. 17th St., Philadelphia 3.
Place: Chicago. Time: June, 1952.

SECTIONAL

Central States Dermatological Association

Harold N. Cole, President, 1422 Euclid Ave., Cleveland 15.

Long Island Dermatologic Society

Ida J. Mintzer, President, 88-50 163d St., Jamaica 3.
Conrad Stritzler, Secretary, 90-26 148th St., Jamaica 2.

New England Dermatological Society

Francis P. McCarthy, President, 371 Commonwealth Ave., Boston.
Leonard E. Anderson, Secretary, Professional Bldg., Springfield, Mass.
Place: New Haven Hospital, New Haven, Conn., and Massachusetts General and Boston City hospitals (in alternation), Boston.

Northern New Jersey Dermatological Society

John P. Kiley, President, 94 Park St., Montclair.
Henri E. Abel, Secretary, 339 Union Ave., Elizabeth.
Place: Academy of Medicine, Newark. Time: 8:00 p. m., second Tuesday in October, November, January, March, and May.

Pacific Dermatological Association

Harry J. Templeton, President, 3115 Webster St., Oakland, Calif.
Walter R. Nickel, Secretary, 233 "A" St., San Diego, Calif.
Place: Oakland, Calif.

Pacific Northwest Dermatological Society

Sam E. Light, President, Medical Arts Bldg., Tacoma, Wash.
Leon F. Ray, Secretary, 628 Medical Dental Bldg., Portland 5, Ore.
Place: Place varies. Time: Third Thursday of May and October.

Rocky Mountain Dermatologic Society

G. P. Lingenfelter, President, 910 Republic Bldg., Denver.
David J. Musman, Secretary, 1024 Republic Bldg., Denver.
Place: Selected prior to each meeting. Time: Selected prior to each meeting.

Southeastern Dermatological Association

C. A. Andrews, Chairman, 706 Franklin St., Tampa, Fla.
Joseph Farrington, Secretary, 204 Laura St., Jacksonville, Fla.

Southern Medical Association, Section on Dermatology and Syphilology

Richard W. Fowlkes, President, 701 Professional Bldg., Richmond 19, Va.
D. Truett Gandy, Secretary, 424 Medical Arts Bldg., Houston 2, Texas.

Southwestern Dermatological Society

Leslie M. Smith, President, First National Bank Bldg., El Paso, Texas.
George K. Rogers, Secretary, Lois Grunow Memorial, Phoenix, Ariz.

STATE

Alabama Dermatological Society

Ray J. Noojin, President, 620 S. 20th St., Birmingham.
James S. Snow, Secretary, First National Bank Bldg., Tuscaloosa.
Time: Fourth Monday of each month, September to May.

Arkansas Dermatological Society

Davis W. Goldstein, Chairman, Cooper Clinic, Fort Smith.
Ray Fulmer, Secretary, 103 E. Seventh St., Little Rock.

California Medical Association, Scientific Assembly, Dermatology and Syphilology Section

Maximilian E. Obermayer, President, 2007 Wilshire Blvd., Los Angeles 5.
Werner W. Duemling, Secretary, 3367 Fourth Ave., San Diego.

Connecticut State Medical Society, Section on Dermatology

William B. Swarts, President, Warwick Towers, Greenwich.
Carter L. Marshall, Secretary, 1488 Chapel St., New Haven.
Place: New Haven.

Florida Association of Dermatology and Syphilology

Wesley W. Wilson, President, 1122 Citizens Bldg., Tampa.
Morris Waisman, Secretary, 1201 Citizens Bldg., Tampa.

Hawaii Dermatological Society

Harry L. Arnold Jr., Secretary, 881 S. Hotel St., Honolulu 53.
Place: 881 S. Hotel St., Honolulu. Time: Every three months when possible.

Indiana State Dermatological Society

Daniel Tweedal, President, 2114 Franklin St., Evansville 12.
Robert E. Jenkins, Secretary, Indianapolis General Hospital, Indianapolis 7.

Louisiana Dermatologic Society

V. Medd Henington, Chairman, 1010 American Bank Bldg., New Orleans.
Raphael Ross Jr., Secretary, 1010 American Bank Bldg., New Orleans.
Place: Charity Hospital, New Orleans. Time: Fourth Sunday of each month.

Massachusetts Medical Society, Section on Dermatology and Syphilology

Austin W. Cheever, President, 464 Beacon St., Boston.
Maurice M. Tolman, Secretary, 636 Beacon St., Boston.
Place: Hotel Statler, Boston.

Medical Society of the State of New York, Section on Dermatology and Syphilology

Maurice J. Costello, President, 140 E. 54th St., New York 22.
William F. Hoover, Secretary, 11 Physicians Bldg., Jamestown.

Medical Society of the State of Pennsylvania, Section on Dermatology

Herman Beerman, President, 255 S. 17th St., Philadelphia.
Thomas Butterworth, Secretary, 411 Walnut St., Reading.

Michigan State Medical Society, Section on Dermatology and Syphilology

John H. Cobane, President, 10 Peterboro, Detroit 1.
Herbert H. Holman, Secretary, 2010 David Broderick Tower, Detroit 26.

Minnesota Dermatological Society

Stephan Epstein, President, 807 W. Fifth St., Marshfield, Wis.
Harold G. Ravits, Secretary, 546 Lowry Medical Arts Bldg., St. Paul.

Rhode Island Dermatological Society

Francesco Ronchese, President, 170 Waterman St., Providence.
Bencel L. Schiff, Secretary, 251 Broadway, Pawtucket.
Time: Second of November, January and March, each year.

Texas Dermatological Society

William A. Clark, President, 1215 Walker Ave., Houston 2.
W. Harris Connor, Secretary, 1215 Walker Ave., Houston 2.
Place: Rotating. Time: Spring, coincident with Texas State Medical Association; fall, October.

LOCAL

Baltimore-Washington Dermatological Society

Lawrence B. McCaleb, Chairman, 1834 K St. N.W., Washington.
Israel Zeligman, Secretary, 1109 N. Calvert St., Baltimore 2.
Place: Baltimore and Washington. Time: Third Thursday of each month in alternate cities. October to May.

Bronx Dermatological Society

Charles R. Rein, President, 580 Fifth Ave.
Henry Silver, Secretary, 290 West End Ave.
Place: Academy of Medicine. Time: Third Thursday of every month, October to May.

Brooklyn Dermatological Society

I. N. Holtzman, President, 135 Eastern Pkwy. (17).
C. B. Locasto, Secretary, 567 First St. (15).
Place: Brooklyn Hospital Clinic, Ashland Place. Time: 8:30 p. m., third Monday of each month, October to June.

Buffalo-Rochester Dermatological Society

Shepard Quimby, President, 287 Linwood Ave., Buffalo.
Frank A. Dolce, Secretary, 468 Delaware Ave., Buffalo.
Place: Edward J. Meyer Memorial Hospital, Buffalo, and Strong Memorial Hospital, Rochester. Time: Second Tuesday of every month, October to May, inclusive.

Central New York Dermatological Society

Maxwell C. Snider, President, 106 Oak St., Binghamton.
John Copeland, Secretary, 200 Lancaster St., Albany.

Chicago Dermatological Society

Theodore Cornbleet, President, 1819 W. Polk St.
James R. Webster, Secretary, 122 S. Michigan Ave.
Place: Chicago. Time: Third Wednesday of each month except June, July, August, and September.

Cincinnati Society of Dermatology and Syphilology

Lawrence C. Goldberg, President, Doctors Bldg.
John B. Squires, Secretary, 1023 Carew Tower.
Place: Cincinnati General Hospital. Time: 8:15 p. m. first Wednesday of each month, October to May.

Cleveland Dermatological Society

Benjamin Levine, President, 10616 Euclid Ave. (6).
Herbert H. Johnson, Secretary, 10515 Carnegie Ave.

Detroit Dermatological Society

Arthur E. Schiller, President, 2010 David Broderick Tower (26).
Charles J. Courville, Secretary, 1202 Maccabees Bldg. (2).
Place: Local hospitals in Detroit and vicinity. Time: Third Tuesday of each month except June, July, August, and September.

Kansas City Dermatological Society

J. Paul Frick, President, 800 Professional Building, Kansas City, Mo.
David B. Morgan, Secretary, 520 Professional Bldg., Kansas City 6, Mo.
Place: University of Kansas Medical Center, Kansas City, Kan. Time: 10:00 a. m., second Sunday of each month, from October through June.

Los Angeles Dermatological Society

Molleurus Couperus, President, 1930 Wilshire Blvd. (5).
Ben A. Newman, Secretary, 6333 Wilshire Blvd.
Place: Good Hope Clinical Association. Time: Second Tuesday of each month, October to May.

Manhattan Dermatologic Society

Herman Sharlit, President, 32 E. 64th St. (21).
George M. Lewis, Secretary, 66 E. 66th St. (21).
Place: Each member's office, in rotation. Time: 8:00 p. m., second Tuesday of each month.

Metropolitan Dermatological Society

Joseph C. Amersbach, President, 105 E. 53d St., New York.
Valentine C. Baker, Secretary, 619 W. 140th St., New York.
Place: Offices of members. Time: Third Monday of each month, October to May.

Metropolitan Dermatological Society of Chicago

Theodore K. Lawless, President, 4321 S. South Pkwy.
Tibor Benedek, Secretary, 25 E. Washington St.
Place: Chicago, alternating in the Services of the Fellows. Time: Second Wednesday, 10:00 a. m., from October through May.

Metropolitan Dermatological Society of Los Angeles

Henry Gordon Morgan, President, 1136 W. Sixth St. (5).
Stanton B. May, Secretary, 119 N. Central Ave., Glendale 3, Calif.
Time: Fourth Tuesday of each month, October through May.

Montreal Dermatological Society

Georges Leclerc, President, 418 Sherbrooke St. E.
R. Roy Forsey, Secretary, 1414 Drummond St.
Place: Royal Victoria Hospital, Notre Dame Hospital, Montreal General Hospital, and other hospitals. Time: October, February, and April.

New York Academy of Medicine, Section of Dermatology and Syphilology

Paul Gross, President, 35 E. 84th St.
Anthony C. Cipollaro, Secretary, 40 E. 61st St. (21).
Place: New York Academy of Medicine, 2 E. 103d St. Time: First Tuesday of each month.

New York Dermatological Society

Anthony C. Cipollaro, Secretary, 40 E. 61st St. (21).
Place: New York. Time: Fourth Tuesday of each month.

Omaha Dermatological Society

Zeno K. Korth, President, 1319 Medical Arts Bldg.
George F. Pinne, Secretary, 453 Aquila Ct.
Time: Third Wednesday of each month, September to June.

Philadelphia Dermatological Society

Edward F. Corson, Chairman, 136 S. 16th St. (2).
H. E. Twining, Secretary, 2026 Delancey Pl. (3).
Place: Philadelphia hospitals. Time: Third Friday of each month except June, July, and August.

Pittsburgh Dermatological Society

H. W. Woolhandler, President, Jenkins Arcade.
P. V. Graham, Secretary, 40 14th St., Wheeling, W. Va.
Place: Falk Clinic, 3601 Fifth Ave. Time: Evening of third Thursday of each month except July and August.

San Francisco Dermatological Society

Stuart C. Way, 490 Post St.
Rees B. Rees, Secretary, 384 Post St.

St. Louis Dermatological Society

Joseph Grindon Jr., President, 539 N. Grand Ave. (3).
Morris Moore, Secretary, 3427 Washington Blvd.
Place: Barnard Free Skin and Cancer Hospital. Time: 8:00 p. m., third Monday of each month, October to May.

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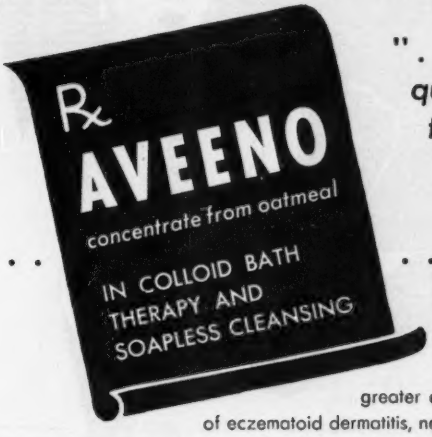

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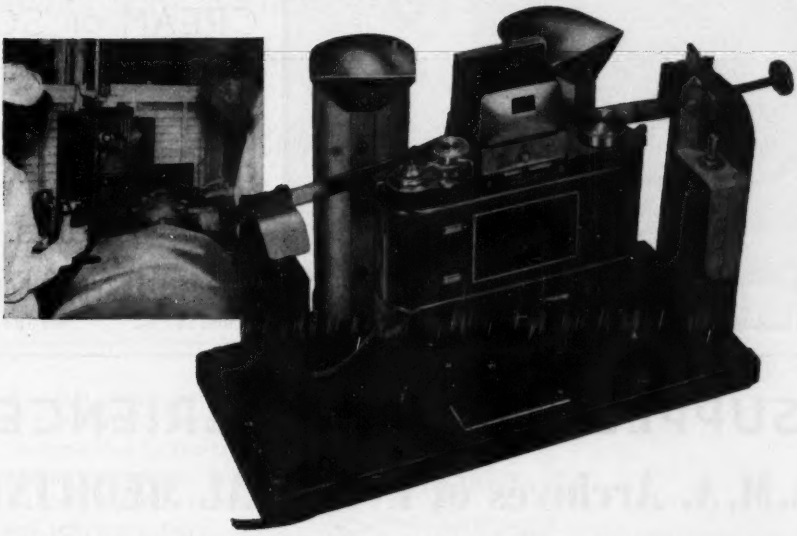

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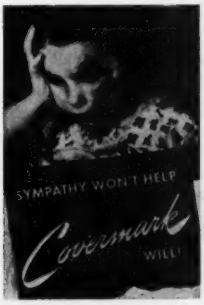

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